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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: R GITOMER Examiner #: 69630 Date: 3/11/02
Art Unit: 1623 Phone Number 30 8-0732 Serial Number: 09/918,234
Mail Box and Bldg/Room Location: 8B19 7A11 Results Format Preferred (circle): PAPER DISK E-MAIL

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

JAN

Jan Delaval
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Searcher Phone #: 4498	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up: 3/18/02	Bibliographic	✓	Dr.Link	
Date Completed: 3/18/02	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	Fulltext		Sequence Systems	
Clerical Prep Time: 30	Patent Family		WWW/Internet	
Online Time: +90	Other		Other (specify)	

PTO-1590 (8-01)

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http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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=> d ide can 13

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   9012-42-4  REGISTRY
CN   Cyclase, adenylate (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Adenyl cyclase
CN   Adenylate cyclase
CN   Adenylyl cyclase
CN   E.C. 4.6.1.1
MF   Unspecified
CI   MAN
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
       CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, EMBASE,
       IFICDB, IFIPAT, IFIUDB, IPA, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
          18645 REFERENCES IN FILE CA (1967 TO DATE)
             42 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          18651 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  136:182399

REFERENCE   2:  136:181653

REFERENCE   3:  136:179700

REFERENCE   4:  136:179596

REFERENCE   5:  136:178618
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REFERENCE 6: 136:178328

REFERENCE 7: 136:178306

REFERENCE 8: 136:178256

REFERENCE 9: 136:178255

REFERENCE 10: 136:178252

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FILE COVERS 1907 - 18 Mar 2002 VOL 136 ISS 12
FILE LAST UPDATED: 17 Mar 2002 (20020317/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> d all tot l76

L76 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:107680 HCAPLUS
DN 136:145271
TI Marker for **antidepressant** therapy and methods related thereto
IN **Rasenick, Mark M.; Donati, Robert J.; Toki, Sadamu**
PA The Board of Trustess of the University of Illinois, USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-566
CC 1-11 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002010763	A2	20020207	WO 2001-US23851	20010730

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-221874P P 20000729

AB The present invention relates generally to methods for detg. the effectiveness of ongoing **antidepressant** therapy via anal. of the assocd. of **Gs.alpha.** with components of the **plasma membrane** or **cytoskeleton** of **cells** from **peripheral** tissues of the **depressed** individual as well as to methods involved in screening for effective **antidepressant** agents via their ability to cause a difference in the assocn. of **Gs.alpha.** with components of the **plasma membrane** or **cytoskeleton** of **cells.**

ST **GSalpha adenylyl cyclase** marker **antidepressant** therapy

IT **G proteins (guanine nucleotide-binding proteins)**
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)
(**Gs (adenylate cyclase-stimulating); plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT Nerve
(neuron; **plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT **Antidepressants**
Drug screening
Erythrocyte
Leukocyte
Neuroglia
Platelet (blood)
(**plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT **Fibroblast**
(**skin; plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT **9012-42-4**
RL: ANT (Analyte); ANST (Analytical study)
(**plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline 50-53-3, Chlorpromazine, biological studies 5560-72-5, Iprindole 54910-89-3, Fluoxetine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

L76 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:402217 HCAPLUS
DN 135:205470
TI Chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs.alpha.**
AU **Donati, Robert J.**; Thukral, Chandrashekhar; **Rasenick, Mark M.**
CS Departments of Physiology and Biophysics, College of Medicine, University of Illinois at Chicago, Chicago, IL, USA
SO Molecular Pharmacology (2001), 59(6), 1426-1432
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
CC 1-11 (Pharmacology)
AB Previous studies have demonstrated that chronic treatment of C6 glioma **cells** with the **antidepressants** desipramine and fluoxetine increases the Triton X-100 soly. of the **G protein Gs.alpha.**. The **antidepressants** also caused a 50% decrease in the amt. of **Gs.alpha.** localized to caveolae-enriched **membrane** domains. In this study, laser scanning confocal microscopy reveals that **Gs.alpha.** is localized to the **plasma membrane** as well as the cytosol in both treated and control **cells**. However, striking differences are seen in the distribution of **Gs.alpha.** in the long cellular processes after chronic treatment with these **antidepressant** drugs. Control **cells** display **Gs.alpha.** along the entire process with an esp. high concn. of that **G protein** at the distal ends. Desipramine- or fluoxetine-treated **cells** show a more centralized clustering of **Gs. alpha.** in the Golgi region of the **cell** and a drastic redn. of **Gs.alpha.** in the cellular processes. There is no change in the distribution of Go.**alpha.** after desipramine treatment and the antipsychotic drug chlorpromazine does not alter **Gs.alpha.**. These results suggest that **antidepressant**-induced changes in the assocn. of **Gs. alpha.** with the **plasma membrane** may translate into altered cellular localization of this signal transducing **protein**. Thus, modification of the coupling between **Gs** -coupled receptors and **adenylyl cyclase** may underlie both **antidepressant** therapy and **depressive** illnesses. This report also suggests that modification of the **membrane** domain occupied by **Gs.alpha.** might represent a mechanism for chronic **antidepressant** effects.
ST **antidepressant G protein Gsalpha** membrane signaling
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**Gs (adenylate cyclase-stimulating), .alpha.**; chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs.alpha.**)
IT **Antidepressants**
Cell membrane
Cytoskeleton
Signal transduction, biological
(chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs .alpha.**)
IT Cytoplasm
(cytosol; chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs .alpha.**)
IT 50-47-5, Desipramine 50-53-3, Chlorpromazine, biological studies

54910-89-3, Fluoxetine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs .alpha.**)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L76 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:659522 HCAPLUS
DN **131:281588**
TI Diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP
IN Chen, Hong; Freimer, Nelson B.
PA Millennium Pharmaceuticals, Inc., USA; The Regents of the University of California
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12P019-34

ICS C12Q001-68; G01N033-53
CC 1-11 (Pharmacology)
Section cross-reference(s): 3, 13
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9951762	A1	19991014	WO 1999-US7401	19990402
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9934696	A1	19991025	AU 1999-34696	19990402
	EP 1068347	A1	20010117	EP 1999-916355	19990402
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1998-80570P	P	19980403		
	WO 1999-US7401	W	19990402		

AB The present invention relates to the mammalian PACAP gene and the discovery that the PACAP gene is linked to the short arm of chromosome 18 in a region of the chromosome involved in mediating neuropsychiatric disorders such as bipolar-affective disorder. The invention relates to methods for the identification of compds. that modulates the expression of PACAP and to using such compds. as therapeutic agents in the treatment of PACAP disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of PACAP-mediated disorders, and to methods and compns. for the treatment of these disorders. The invention also relates to use of the PACAP gene and/or gene products as markers for fine structure mapping of a region of human chromosome 18, including a region of the chromosome involved in mediating neuropsychiatric disorders.

ST pituitary **adenylate cyclase** activating peptide gene neuropsychiatric disorder; PACAP gene mapping neuropsychiatric disorder diagnosis treatment

IT Gene, animal
RL: ANT (Analyte); BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(PACAP; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)

IT Mutation
(deletion, diagnosis by detection of; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)

IT Drug screening
Genetic mapping
Mental disorder
Nucleic acid amplification (method)
Nucleic acid hybridization
Psychotropics
Schizophrenia
Susceptibility (genetic)
(diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)

IT cDNA sequences
(for human pituitary **adenylate cyclase**-activating peptide)

IT Diagnosis
(genetic; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating

peptide gene PACAP)
IT Chromosome
(human 18; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
IT Mutation
(insertion, diagnosis by detection of; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
IT **Mental disorder**
(**mania**; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
IT **Mental disorder**
(**manic bipolar disorder**; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
IT DNA sequences
(of human gene PACAP encoding pituitary **adenylate cyclase**-activating peptide)
IT Protein sequences
(of human pituitary **adenylate cyclase**-activating peptide)
IT Mutation
(substitution, diagnosis by detection of; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
IT **134688-73-6 245755-73-1**
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase** -activating peptide gene PACAP)
IT **137061-48-4**, Pituitary **adenylate cyclase** -activating peptide
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
IT 9075-08-5, Restriction endonuclease
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
IT **246038-54-0**
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase** -activating peptide gene PACAP)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L76 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:547159 HCAPLUS
DN **131:270413**
TI **G protein**-coupled cyclic AMP signaling in postmortem brain of subjects with mood disorders: effects of diagnosis, suicide, and treatment at the time of death
AU Dowlatshahi, Dar; MacQueen, Glenda M.; Wang, Jun-Feng; Reiach, James S.;

Young, L. Trevor
CS Mood Disorders Program, McMaster University, Hamilton, ON, L8N 3Z5, Can.
SO J. Neurochem. (1999), 73(3), 1121-1126
CODEN: JONRA9; ISSN: 0022-3042
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
AB Components of cAMP signaling were examd. in postmortem cerebral cortex of a well characterized group of patients with mood disorders and nonpsychiatric control subjects. We measured **G protein** levels, **adenylyl cyclase** (AC) activity, and CREB levels in cerebral cortex of the subjects with respect to diagnosis, treatment, and suicide. There was no effect of diagnosis on any measure, except for a trend toward decreased **stimulated** AC activity in subjects with mood disorders relative to control subjects. We also detected a significant effect of suicide on temporal cortex CREB levels in subjects that died as a result of suicide relative to those that did not, which was more evident in patients with major **depressive** disorder. Bipolar disorder (BD) subjects treated with anticonvulsants at the time of death had decreased temporal cortex CREB levels relative to those not receiving anticonvulsants. Furthermore, we found a trend toward decreased occipital cortex **G.alpha**.s (short) levels in BD subjects treated with lithium. These results support the hypothesis of altered cAMP signaling in mood disorders and raise the possibility that factors other than diagnosis, such as treatment and suicide, may be relevant to **cell**-signaling abnormalities reported in the literature.
ST suicide **depression** brain cAMP signaling
IT Transcription factors
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(CREB (cAMP-responsive element-binding); **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT Second messenger system
(**G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT **G proteins (guanine nucleotide-binding proteins)**
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**Gs (adenylate cyclase-stimulating), .alpha.** subunit; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT Brain
(cerebral cortex; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT **Mental disorder**
(**depression**, major; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT Anticonvulsants
(effect on temporal cortex CREB levels in humans with bipolar disorder)

IT **Mental disorder**
(**manic bipolar disorder**; CREB levels in temporal cortex of humans with)

IT **Mental disorder**
(mood-affecting; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT Brain

(occipital cortex; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
IT Death
(suicide; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
IT Brain
(temporal cortex; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
IT **9012-42-4, Adenylyl cyclase**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
IT 60-92-4, CAMP
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L76 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:547158 HCAPLUS
DN 131:281415
TI Treatment of C6 glioma **cells** and rats with **antidepressant** drugs increases the detergent extraction of **Gs.alpha.** from **plasma membrane**
AU **Toki, Sadamu; Donati, Robert J.; Rasenick, Mark M.**
CS Departments of Physiology and Biophysics, University of Illinois College of Medicine, Chicago, IL, 60612-7342, USA
SO J. Neurochem. (1999), 73(3), 1114-1120
CODEN: JONRA9; ISSN: 0022-3042
PB Lippincott Williams & Wilkins
DT Journal
LA English

CC 1-11 (Pharmacology)
AB Results from previous studies suggested that chronic treatment of rats or C6 glioma **cells** with **antidepressants** augments the coupling between **Gs** and **adenylyl cyclase**. As these effects on C6 glioma **cells** are seen in the absence of presynaptic input, several **antidepressant** drugs may have a direct "postsynaptic" effect on their target **cells**. It was hypothesized that the target of **antidepressant** action was some **membrane protein** that may regulate coupling between **G proteins** and **adenylyl cyclase**. To test this, C6 glioma **cells** were treated with amitriptyline, desipramine, iprindole, or fluoxetine for 3 days. Chlorpromazine served as a control for these treatments. **Membrane proteins** were extd. sequentially with Triton X-100 and Triton X-114 from C6 glioma **cells**. Triton X-100 extd. more **Gs.alpha.** in **membranes** prepd. from **antidepressant**-treated C6 glioma **cells** than from control groups. In addn., **cell** fractionation studies revealed that the amt. of **Gs.alpha** . in caveolin-enriched domains was reduced after **antidepressant** treatment and that **adenylyl cyclase** comigrated with **Gs.alpha.** in the gradients. These data suggest that some postsynaptic component that increases availability of **Gs** to activate effector mols., such as **adenylyl cyclase**, might be a target of **antidepressant** treatment.
ST **antidepressant G protein adenylyl cyclase** signaling
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**adenylate cyclase**-regulating; **antidepressant** drug mechanism of action: **Gs .alpha.-adenylyl cyclase** signaling mediation)
IT **Antidepressants**
Signal transduction, biological
(**antidepressant** drug mechanism of action: **Gs .alpha.-adenylyl cyclase** signaling mediation)
IT **Proteins**, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(membrane; **antidepressant** drug mechanism of action: **Gs.alpha.-adenylyl cyclase** signaling mediation)
IT 50-47-5, Desipramine 50-48-6, Amitriptyline 5560-72-5, Iprindole 54910-89-3, Fluoxetine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antidepressant** drug mechanism of action: **Gs .alpha.-adenylyl cyclase** signaling mediation)
IT **9012-42-4, Adenylyl cyclase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**antidepressant** drug mechanism of action: **Gs .alpha.-adenylyl cyclase** signaling mediation)
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L76 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:150163 HCAPLUS
DN 131:13783
TI Alterations of tubulin function caused by chronic **antidepressant** treatment in rat brain
AU Kamada, Hiroki; Saito, Toshikazu; Hatta, Shinichi; **Toki, Sadamu**; Ozawa, Hiroki; Watanabe, Masayuki; Takahata, Naohiko
CS Department of Neuropsychiatry, School of Medicine, Sapporo Medical University, Sapporo, 060-8556, Japan
SO Cell. Mol. Neurobiol. (1999), 19(1), 109-117
CODEN: CMNEDI; ISSN: 0272-4340
PB Kluwer Academic/Plenum Publishers
DT Journal
LA English
CC 1-11 (Pharmacology)
AB **Antidepressants** have been used clin. for many years; however, the neurochem. mechanism for their therapeutic effect has not been clarified yet. Recent reports indicate that chronic **antidepressant** treatment directly affects the postsynaptic membrane to increase the coupling between the **stimulatory** GTP-binding (**G**) **protein**, **Gs**, and **adenylyl cyclase**. Tubulin, a **cytoskeletal** element, is involved in the **stimulatory** and inhibitory regulation of **adenylyl cyclase** in rat cerebral cortex via direct transfer of GTP to **G proteins**. In this study, the authors investigated whether the functional change of the **adenylyl cyclase** system caused by chronic **antidepressant** treatment involves an alteration of tubulin function in the regulation of **adenylyl cyclase** activity. Male Sprague-Dawley rats were treated once daily with amitriptyline or saline by i.p. injection (10 mg/kg) for 21 days, and their cerebral cortex membranes and GppNHp-liganded tubulin (tubulin-GppNHp) were prepd. for what. GppNHp-**stimulated** **adenylyl cyclase** activity in cortex membranes from amitriptyline-treated rats was significantly higher than that in control membranes. Furthermore, tubulin-GppNHp prepd. from amitriptyline-treated rats was more potent than that from control rats in the **stimulation** of **adenylyl cyclase** activity in the cortex membranes of the controls. However, there was no significant difference in manganese-**stimulated adenylyl** **cyclase** activity between control and amitriptyline-treated rats. The present results suggest that chronic **antidepressant** treatment enhances not only the coupling between **Gs** and the catalytic subunit of **adenylyl cyclase** but also tubulin interaction with **Gs** in the cerebral cortex of the rat.
ST tubulin function alteration **antidepressant** brain

IT Proteins, specific or class
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(GTP-binding; alterations of tubulin function caused by chronic **antidepressant** treatment in brain)
IT **Antidepressants**
(alterations of tubulin function caused by chronic **antidepressant** treatment in brain)
IT Tubulins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(alterations of tubulin function caused by chronic **antidepressant** treatment in brain)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(alterations of tubulin function caused by chronic **antidepressant** treatment in brain)
IT Brain
(cerebral cortex; alterations of tubulin function caused by chronic **antidepressant** treatment in brain)
IT 50-48-6, Amitriptyline
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(alterations of tubulin function caused by chronic **antidepressant** treatment in brain)
IT **9012-42-4, Adenylyl cyclase**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); BIOL (Biological study)
(alterations of tubulin function caused by chronic **antidepressant** treatment in brain)
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L76 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:31135 HCAPLUS
DN 126:69607
TI **G protein**-mediated signal transduction as a target of **antidepressant** and antibipolar drug action: evidence from model

systems
AU **Rasenick, Mark M.**; Chaney, Kimberly A.; Chen, Jiang
CS College Medicine, University Illinois, Chicago, IL, 60612-7342, USA
SO J. Clin. Psychiatry (1996), 57(Suppl. 13), 49-58
CODEN: JCLPDE; ISSN: 0160-6689
PB Physicians Postgraduate Press
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A **review**, with 38 refs., discussing evidence that altered **G protein**-mediated signal transduction provides at least one piece with which to complete the mosaic defining the cascade of mol. events resulting in **antidepressant** or antimanic action. It is demonstrated that simple, exptl. accessible systems represent ideal models with which to det. the nature of candidate **antidepressant** or antimanic compds.
ST **review G protein antidepressant** mania therapy; signal transduction **antidepressant** mania therapy **review**; bipolar disease therapy **G protein review**
IT **Antidepressants**
Bipolar disorder
Mania
Signal transduction (biological)
(**G protein**-mediated signal transduction as a target of **antidepressant** and antibipolar drug action)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(signal transduction mediated by **G proteins** as a target of **antidepressant** and antibipolar drug action)
IT Biological simulation
(signal transduction mediated by **G proteins** as a target of **antidepressant** and antibipolar drug action as studied by)

L76 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:886523 HCAPLUS
DN 123:306475
TI Chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content
AU Chen, Jiang; **Rasenick, Mark M.**
CS Dep. Physiology Biophys., Univ. Illinois Coll. Med., Chicago, USA
SO J. Pharmacol. Exp. Ther. (1995), 275(1), 509-17
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
CC 1-11 (Pharmacology)
AB It has been suggested that the mol. basis of **antidepressant** action involves postreceptor components. Results from the studies have suggested that a **G protein** (**Gs**) is one of those targets and that chronic **antidepressant** treatment facilitates the activation of **adenylyl cyclase** by **GS.alpha.**. This report represents an attempt to define which aspects of **G protein** function are altered by chronic **antidepressant** treatment. Rats were treated for 21 days with amitriptyline, desipramine, ABT 200 (a pyrollidine with putative **antidepressant** effects) or electroconvulsive shock, and membranes were prepd. from the cerebral cortexes. Each of these treatments caused an increase in membrane **adenylyl cyclase** assayed in the presence of guanyl-5'-imidodiphosphate (.gtoreq. 1 .mu.M). Results of acute **antidepressant** treatments were no different than those of control treatment. Chronic treatment with amphetamine, which inhibits neurotransmitter reuptake without displaying **antidepressant** effect, was also ineffective in increasing **Gs.alpha.** **stimulation** of **adenylyl cyclase**. Chronic

antidepressant treatment did not change the content of **G protein**, as no change at the level of **Gs.alpha**., Gi.**alpha**., Go.**alpha**. or **G**.beta. **protein** was detected by immunoblotting. Although there was no change in the amt. of **G proteins**, **antidepressant** treatment increased the no. of active **Gs**. **alpha**./**adenylyl cyclase** complexes immunopptd. by an anti-**Gs.alpha**. antibody. It is suggested that chronic **antidepressant** treatment alters certain membrane components such that a greater proportion of **Gs.alpha**. is activated, **Gs.alpha**. enjoys a more fruitful interaction with **adenylyl cyclase**, or both.

ST **antidepressant G protein adenylyl cyclase** brain

IT **Antidepressants**
Cell membrane
(chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT **G proteins (guanine nucleotide-binding proteins)**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT Brain
(cerebral cortex, chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT Convulsion
(electro-, chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline 148152-63-0, ABT 200
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT **9012-42-4, Adenylyl cyclase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

L76 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:318539 HCAPLUS
DN 122:96306
TI Chronic treatment of C6 glioma **cells** with **antidepressant** drugs increases functional coupling between a **G protein** (**Gs**) and **adenylyl cyclase**
AU Chen, Jiang; **Rasenick, Mark M.**
CS Dep. Physiol., Univ. Illinois Coll. Med., Chicago, IL, USA
SO J. Neurochem. (1995), 64(2), 724-32
CODEN: JONRA9; ISSN: 0022-3042
DT Journal
LA English
CC 1-11 (Pharmacology)
AB It has been reported that **antidepressant** treatment in rats results in a significant increase of **Gs**-mediated **stimulation** of **adenylyl cyclase** and this effect correlates well with the clin. therapeutic response. This increased activity occurs despite a down-regulation of several receptors linked normally to the **stimulation** of that enzyme. To distinguish between these effects and to det. whether presynaptic components of the **cell** are required, C6 glioma **cells**

were treated with **antidepressants**. Tricyclic (amitriptyline and desipramine) or atypical (iprindole) **antidepressant** exposure to C6 **cells** for 5 days significantly increased guanylyl-5'-imidodiphosphate [Gpp(NH)p]-**stimulated adenylyl cyclase** activity in **membrane** prepns. in a manner similar to that seen for rat brain **membranes** after 21-day treatment. This effect was drug dose and exposure time dependent. Nevertheless, **stimulation** of **adenylyl cyclase** by isoproterenol was decreased after **antidepressant** treatment. By comparison, the **antidepressant**-induced .beta.-receptor desensitization occurred earlier than the enhancement of Gpp(NH)p-activated **adenylyl cyclase**, and extensive desensitization of .beta. receptors by isoproterenol treatment did not enhance the Gpp(NH)p-**stimulated adenylyl cyclase** activity. These results indicated that the **antidepressants** have a direct effect on **cell** signaling and this enhanced Gpp(NH)p-**stimulated adenylyl cyclase** activity is not correlated with desensitization of .beta.-adrenergic receptor **stimulated adenylyl cyclase**. These data contribute to the suggestion that **G proteins** (esp. **Gs**) are the target of **antidepressant** actions. Immunoblotting showed that neither the no. of **G protein** subunits (.**alpha**.s, .**alpha**.i, .**alpha**.0, and .beta.) nor their assocn. with the **plasma membrane** was changed after **antidepressant** treatment. Thus, these results are consistent with the hypothesis that chronic **antidepressant** treatment acts directly at the postsynaptic **membrane** to increase the coupling between **Gs** and **adenylyl cyclase**.

ST **antidepressant G protein adenylyl cyclase** coupling; glioma **antidepressant G protein adenylyl cyclase**

IT **Antidepressants**
(chronic treatment of C6 glioma **cells** with **antidepressant** drugs increases functional coupling between **G protein** (**Gs**) and **adenylyl cyclase**)

IT **G proteins (guanine nucleotide-binding proteins)**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**Gs** (**adenylate cyclase-stimulating**), chronic treatment of C6 glioma **cells** with **antidepressant** drugs increases functional coupling between **G protein** (**Gs**) and **adenylyl cyclase**)

IT Neuroglia
(neoplasm, chronic treatment of C6 glioma **cells** with **antidepressant** drugs increases functional coupling between **G protein** (**Gs**) and **adenylyl cyclase**)

IT Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.beta.-adrenergic, chronic treatment of C6 glioma **cells** with **antidepressant** drugs increases **adenylyl cyclase** activity in relation to desensitization of .beta.-adrenergic receptors)

IT 34273-04-6, Guanylyl-5'-imidodiphosphate
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(chronic treatment of C6 glioma **cells** with **antidepressant** drugs increases Gpp(NH)p-**stimulated adenylyl cyclase**)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline 5560-72-5, Iprindole
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic treatment of C6 glioma **cells** with **antidepressant** drugs increases functional coupling between

G protein (**Gs**) and **adenylyl cyclase**)

L76 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:667983 HCAPLUS
DN 119:267983
TI Cerebral cortex **Gs.alpha. protein** levels and forskolin-**stimulated** cyclic AMP formation are increased in bipolar affective disorder
AU Young, L. Trevor; Li, Peter P.; Kish, Stephen J.; Siu, Kin Po; Kamble, Arvind; Hornykiewicz, Oleh; Warsh, Jerry J.
CS Sect. Biochem. Psychiatry, Clarke Inst. Psychiatry, Toronto, ON, M5T 1R8, Can.
SO J. Neurochem. (1993), 61(3), 890-8
CODEN: JONRA9; ISSN: 0022-3042
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
AB Exptl. animal and **peripheral blood cell** studies point to guanine nucleotide regulatory (**G**) **protein** disturbances in bipolar affective disorder. The authors have previously reported elevated prefrontal cortex **Gs. alpha. protein** in bipolar affective disorder and have now extended these preliminary observations in a larger no. of subjects, assessing the brain regional specificity of these changes in greater detail, detg. the functional biochem. correlates of such changes, and evaluating their diagnostic specificity. **Membrane G protein** (**Gs.alpha.**, Gi.**alpha.**, Go. **alpha.**, and **G**.beta.) immunoreactivities were estd. by western blotting in postmortem brain regions obtained from 10 patients with a DSMIII-R diagnosis of bipolar affect disorder and 10 nonpsychiatric controls matched on the basis of age, postmortem brain regions obtained from 10 patients with a DSMIII-R diagnosis of bipolar affective disorder and 10 nonpsychiatric controls matched on the basis of age, postmortem delay, and brain pH. To examine whether there were functional correlates to the obsd. elevated **Gs.alpha.** levels, basal and GTP.gamma.S- and forskolin-**stimulated** cAMP prodn. was detd. in the same brain regions. Compared with controls, **Gs. alpha.** (52-kDa species) immunoreactivity was significantly ($p < 0.05$) elevated in prefrontal (+36%), temporal (+65%), and occipital (+96%) cortex but not in hippocampus (+28%), thalamus (-23%), or cerebellum (+21%). In contrast, no significant differences were found in the other **G protein** subunits (Gi.**alpha.**, Go. **alpha.**, **G**.beta.) measured in these regions. Forskolin-**stimulated** cAMP prodn. was significantly increased in temporal (+31%) and occipital (+96%) cortex but not in other regions. No significant differences were apparent in basal or GTP.gamma.S-**stimulated** cAMP prodn. A significant correlation was obsd. between forskolin-**stimulated** cAMP formation and **Gs. alpha.** (52 kDa) immunoreactivity when examd. across these cortical regions. The obsd. increase in **Gs.alpha.** may be specific to bipolar disorders as no significant differences were detected in **Gs.alpha.** levels in temporal cortex from patients with either schizophrenia or Alzheimer's disease. In summary, the present study confirms and extends the authors' earlier findings and supports the notion that increased **Gs.alpha.** levels and possibly **Gs.alpha.**-**adenylyl cyclase**-mediated signal transduction are relevant to the pathophysiol. of bipolar affective disorder.
ST affective disorder brain **Gs protein**
IT Signal transduction, biological
(**G protein**-mediated, in brain regions, in bipolar affective disorder of humans)
IT Brain, composition
(**Gs.alpha. protein** levels and cAMP formation in regions of, in bipolar affective disorders of humans)

IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(**G**.beta., of brain regions, in bipolar affective disorders of humans)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(Gi (**adenylate cyclase**-inhibiting), .**alpha**.-subunit, of brain regions, in bipolar affective disorders of humans)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(Go, .**alpha**.-subunit, of brain regions, in bipolar affective disorders of humans)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(**Gs** (**adenylate cyclase-stimulating**), .**alpha**.-subunit, of brain regions, in bipolar affective disorders of humans)
IT **Mental disorder**
(**manic depression, Gs.alpha. proteins** and cAMP formation increase in brain regions in, in humans)
IT 60-92-4, CAMP
RL: FORM (Formation, nonpreparative)
(formation of, increase in, in brain regions of humans with bipolar affective disorder)

L76 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:512079 HCAPLUS
DN 115:112079
TI The effects of electroconvulsive shock on receptor-**G protein-adenylate cyclase** coupling
AU Ozawa, Hiroki; **Rasenick, Mark M.**; Takahata, Naohiko; Saito, Toshikazu
CS Dep. Neuropsychiatry, Sapporo Med. Coll., Sapporo, Japan
SO Jpn. J. Psychiatry Neurol. (1991), 45(1), 137-8
CODEN: JJPNEA; ISSN: 0912-2036
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
AB In rats, the long-term administration of electroconvulsive shock (ECS) induced a significant decrease in the no. of brain beta-adrenergic receptors without altering the affinity of the sites. In contrast to the above results, Gpp(NH)p, NaF or forskolin **stimulated adenylate cyclase** (AC) activity was increased in the rat cerebral cortex membranes. These effects by ECS were progressive in a time-dependent manner, but no significant differences were seen in sham or acute treatment. The percent inhibition induced by GppNHp as well as the IC50 for that compd. was equiv. in all the groups and the chem. elimination of GTP-binding **proteins** (**G protein**) abolished the enhancement of AC by the chronic ECS treatment. The dissocn. const. (Kd) and maximal binding (Bmax) for AAGTP (a hydrolysis-resistant, photoaffinity GTP analog) to synaptic membrane **G proteins** was unchanged after the ECS treatment. Thus, it is unlikely that there was any change in the quantity or GTP-binding capacity of **G proteins**. However, the transfer of [32P]-AAGTP from Gi/o to **Gs** was accelerated by the chronic ECS treatment. Treatment alters some aspect of the milieu in which **G proteins** interface with their receptors, effectors and with one another, esp. under a "**G protein**" upon the system. Such neurochem. changes in ECS appear to be similar to those of **antidepressant** drug therapy.
ST electroconvulsive shock receptor **protein adenylate cyclase**; adrenergic beta receptor coupling electroconvulsive shock; **G protein** receptor coupling electroconvulsive shock; **adenylate cyclase** receptor coupling electroconvulsive shock

IT **Proteins, specific or class**
RL: BIOL (Biological study)
(**adenylate cyclase**-regulating, **guanine nucleotide-binding, G,** .beta.-adrenergic receptors coupling with, electroconvulsive shock effect on, in brain)
IT Brain, composition
(cerebral cortex, .beta.-adrenergic-**G protein-adenylate cyclase** system of, electroconvulsive shock effect on)
IT Convulsion
(electro-, .beta.-adrenergic receptor-**G protein-adenylate cyclase** coupling response to, in brain)
IT Receptors
RL: BIOL (Biological study)
(.beta.-adrenergic, **G protein-adenylate cyclase** coupling to, electroconvulsive shock effect on, in brain)
IT **9012-42-4, Adenylate cyclase**
RL: BIOL (Biological study)
(.beta.-adrenergic receptor-**G protein** coupling with, electroconvulsion effect on, in brain)

L76 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:40359 HCAPLUS
DN 114:40359
TI Chronic electroconvulsive treatment augments coupling of the GTP-binding **protein Gs** to the catalytic moiety of **adenylyl cyclase** in a manner similar to that seen with chronic **antidepressant** drugs
AU Ozawa, Hiroki; **Rasenick, Mark M.**
CS Coll. Med., Univ. Illinois, Chicago, IL, 60680, USA
SO J. Neurochem. (1991), 56(1), 330-8
CODEN: JONRA9; ISSN: 0022-3042
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
AB A significant increase of guanylylimidodiphosphate (GppNHp)-, fluoride-, and forskolin-**stimulated adenylyl cyclase** was obsd. in synaptic membrane prepns. from rat cerebral cortex subsequent to chronic electroconvulsive shock (ECS) treatment. This effect required at least five treatments over a course of 10 days. The inhibition of **adenylyl cyclase** induced by GppNHp was not affected by these treatments. The dissocn. const. (kD) and maximal binding for the photoaffinity GTP analog. [32P]P3-(4-azidoanilido)-P1-5'-GTP([32P]AAGTP), to each of the synaptic membrane **G proteins** also were unchanged after ECS treatment. Nonetheless, the transfer of [32P]AAGTP from Gi to **Gs**, which the authors suggest is indicative of the coupling between **Gs** and the **adenylyl cyclase** catalytic moiety, was accelerated by chronic ECS treatment but not by acute or sham treatment. Furthermore, chem. uncoupling of **Gs** from **adenylyl cyclase** rendered membranes from treated animals indistinguishable from controls. Finally, in all cases tested, membranes prepd. from animals subjected to chronic treatment with amitriptyline or iprindole showed similar changes in the **Gs** -mediated activation of **adenylyl cyclase**. Acute treatments produced effects similar to controls, and liver and kidney membranes from animals receiving chronic treatment showed no changes in **adenylyl cyclase** despite the marked changes seen in brain. These results suggest that chronic administration of ECS enhances coupling between **Gs**, and **adenylyl cyclase** enzyme and modifies interactions between **Gs** and Gi.
ST **adenylyl cyclase** binding **G protein** electroconvulsion; **antidepressant adenylyl cyclase** binding **G protein**
IT Synapse

(**adenylyl cyclase** binding by **G proteins** in membranes of, electroconvulsion and **antidepressant** drugs effects on)

IT **Antidepressants**
(**adenylyl cyclase** of synaptic membranes response to electroconvulsion and, mechanism of action in relation to)

IT Phospholipoproteins
RL: BIOL (Biological study)
(**adenylate cyclase**-inhibiting, guanine nucleotide-binding, Gi, **Gs proteins** interactions with, in synaptic membranes, electroconvulsion effect on, mechanism of action of **antidepressant** drugs in relation to)

IT **Proteins, specific or class**
RL: BIOL (Biological study)
(**adenylate cyclase-stimulating, guanine nucleotide-binding, Gs, adenylyl cyclase** binding by, electroconvulsion and **antidepressant** drugs effects on)

IT Convulsion
(electro-, **G protein** binding to **adenylyl cyclase** induced by, in synaptic membranes, mechanism of action of **antidepressant** drugs in relation to)

IT **9012-42-4, Adenylyl cyclase**
RL: BIOL (Biological study)
(**Gs proteins** binding of, in synaptic membranes, electroconvulsion effect on, mechanism of **antidepressant** drugs in relation to)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline 5560-72-5, Iprindole
RL: BIOL (Biological study)
(**adenylyl cyclase** of synaptic membranes response to electroconvulsion and, mechanism of action in relation to)

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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 13 March 2002 (20020313/ED)

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L114 ANSWER 1 OF 36 BIOSIS
AN 2002:158317 BIOSIS
DN PREV200200158317
TI Association of **Gsalpha** with membrane and cytoskeletal components is modified by chronic **antidepressant** treatment.
AU **Donati, Robert J. (1)**; Thukral, Chandreshekar (1); **Rasenick, Mark M.**
CS (1) Physiology and Biophysics, University of Illinois, 835 S. Wolcott, Rm. No. E202, Chicago, IL, 60612 USA
SO Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 412a. http://www.molbiolcell.org/. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology Washington DC, USA December 08-12, 2001
ISSN: 1059-1524.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520**
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Biophysics - Membrane Phenomena *10508
Enzymes - General and Comparative Studies; Coenzymes *10802
Pathology, General and Miscellaneous - Therapy *12512
Pharmacology - General *22002
Pharmacology - Psychopharmacology *22026
IT Major Concepts
Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Pharmacology
IT Parts, Structures, & Systems of Organisms
cytoskeleton; plasma membrane
IT Chemicals & Biochemicals
G-s-**alpha; adenylyl cyclase**: activation;
desipramine: **antidepressant** - drug, chronic treatment;
tubulin
IT Miscellaneous Descriptors
Triton X-100 insoluble membrane domain; Triton X-100 soluble membrane domain; Meeting Abstract
RN **9012-42-4 (ADENYLYL CYCLASE)**
50-47-5 (DESIPRAMINE)

L114 ANSWER 2 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:155052 BIOSIS
DN PREV200200155052
TI **Antidepressant**-induced changes in **Gsalpha** cellular localization may be caused by a disruption of the plasma membrane lipid domain.
AU **Donati, Robert J. (1)**; Thukral, Chandrashekar S.; Shah, Bindu N.; **Rasenick, Mark M.**
CS (1) Physiology and Biophysics, University of Illinois at Chicago, 835 S. Wolcott, Chicago, IL, 60612 USA
SO Molecular Biology of the Cell, (Dec., 2000) Vol. 11, No. Supplement, pp. 340a. http://www.molbiolcell.org/. print.
Meeting Info.: 40th American Society for Cell Biology Annual Meeting San Francisco, CA, USA December 09-13, 2000
ISSN: 1059-1524.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520**
Cytology and Cytochemistry - General *02502
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Lipids *10066
Biochemical Studies - Sterols and Steroids *10067
Physiology, General and Miscellaneous - General *12002
Pathology, General and Miscellaneous - Therapy *12512
Pharmacology - General *22002
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Chemical Coordination and Homeostasis; Pharmacology
IT Parts, Structures, & Systems of Organisms
Golgi
IT Chemicals & Biochemicals
G-proteins: analysis, functions, structures;
Gs-alpha proteins: analysis, cellular localization changes; cholesterol; cyclodextrins; imipramine: adrenergic antagonist - drug, **antidepressant** - drug, autonomic - drug, pharmacodynamics; lipids; plasma membrane lipids: analysis, domain disruption, functions, structures; sphingolipids
IT Miscellaneous Descriptors
signaling; Meeting Abstract
RN 57-88-5 (CHOLESTEROL)
12619-70-4 (CYCLODEXTRINS)
50-49-7 (IMIPRAMINE)

L114 ANSWER 3 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:562372 BIOSIS
DN PREV200100562372
TI **Gsalpha** is a specific target of chronic **antidepressant** treatment.
AU **Donati, R. J. (1)**; Thukral, C. (1); **Rasenick, M. M. (1)**
CS (1) Physiology and Biophysics, University of Illinois College of Medicine, Chicago, IL USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1767. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT **Conference**
LA English
SL English
AB Previous studies in this laboratory have demonstrated that **Gsalpha** from C6 rat glioma cells migrates from a Triton X-100 (TTX-100) insoluble membrane domain (TIMD) to a TTX-100 soluble membrane domain in response to chronic treatment with the **antidepressants** desipramine and fluoxetine (Toki et al., 1999 J. Neurochem. 73(3): 1114-1120). In this same study it was also reported that there was a 50% decrease in the amount of **Gsalpha** localized to caveolae-enriched TTX-100 insoluble membranes. Laser scanning confocal microscopy revealed that **Gsalpha** is localized to the plasma membrane as well as the cytosol in both the desipramine-treated and control cells. However, striking differences were seen in the distribution of **Gsalpha** in the long cellular processes and process tips (Donati et al., 2001 Mol. Pharm. in press). There was no change in the distribution of Goalpha after desipramine treatment. Current studies have focused on examining the localization of other members of the **Gsalpha** signaling cascade to TIMDs before and after desipramine treatment. These results indicate that while there is a 30-40% decrease in **Gsalpha** localized to these membrane domains, the localization of other members of the signaling cascade (**adenylyl cyclase type** V/**VI** , PKA II regulatory and catalytic subunits, and tubulin) remained relatively unchanged. This suggests that **antidepressant**-induced changes in the association of **Gsalpha** with the plasma membrane may be specific to this signal transducing protein and that **Gsalpha** may be a unique target of **antidepressant** action.
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Pathology, General and Miscellaneous - Therapy *12512
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Pharmacology - General *22002
Pharmacology - Psychopharmacology *22026
Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects *24004
BC Muridae 86375
IT Major Concepts
Nervous System (Neural Coordination); Pharmacology
IT Parts, Structures, & Systems of Organisms
caveola; cytosol; plasma membrane
IT Diseases
glioma: neoplastic disease, nervous system disease
IT Chemicals & Biochemicals
Gs-alpha: distribution, localization, signaling;
PKA II [protein kinase A II]: catalytic subunit, localization, regulatory subunit; Triton X-100 insoluble membrane domain [TIMD]; Triton X-100 soluble membrane domain; **adenylyl cyclase type** V/**VI**: localization;

desipramine: **antidepressant** - drug, pharmacodynamics;
tubulin: localization
IT Alternate Indexing
Glioma (MeSH)
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
C6 cell line (Muridae): rat glioma cell
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
Rodents; Vertebrates
RN 50-47-5 (DESIPRAMINE)

L114 ANSWER 4 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:478361 BIOSIS
DN PREV200100478361
TI Alterations in the distribution of **G protein** in the plasma membrane from postmortem brains of **depressive** and schizophrenic.
AU **Toki, S. (1)**; Senda, S.; Ozawa, H. (1); Choei, H. (1); Yamada, S. (1); Saito, T. (1)
CS (1) Neuropsychiatry, Sapporo Medical Univ, Sapporo Japan
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 310. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT **Conference**
LA English
SL English
AB Previous study have suggested that the altered function in the second-messenger system may involve in the etiology of psychiatric disorders. In **depressives**, the attenuation of the **Gs** -mediated **adenylyl cyclase** (AC) activity in the cerebral cortex has been suggested. On the other hand, several investigators have reported the increased AC activity in the brain from the schizophrenics. Recently, it has been suggested that the membrane **proteins** such as **G proteins** and receptors are associated with some cytoskeletal **proteins** that restrict the distribution and mobility of these **proteins** and alteration in the interaction between these components might affect to the second-messenger system. Therefore, we examined the alteration in the distribution of **G proteins** in the plasma membrane from postmortem human brains of patients with psychiatric disorders. Frontal cortex membranes from the post-mortem brains of **depressives**, schizophrenics and controls were examined. Membrane-enriched fractions from each group were prepared from frontal cortex and membrane **proteins** were extracted with detergent (Triton X-100 (TX-100)). The amount of **G protein** in each extract was estimated by immunoblotting. In **depressive** group, TX-100 extracted less amount of **G**(s **alpha**) from the membrane in compare to control group. On the other hand, in the schizophrenic group, TX-100 extracted more **G**(s **alpha**) from the membrane in compare to control group. These change might affect to the coupling between **G protein** and effector. Therefore, these data suggests that the change in the distribution of **G protein** may involve in the etiology of psychiatric disorders.
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520**
Cytology and Cytochemistry - Human *02508
Behavioral Biology - General and Comparative Behavior *07002
Behavioral Biology - Human Behavior *07004
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Membrane Phenomena *10508
Enzymes - General and Comparative Studies; Coenzymes *10802

Nervous System - Physiology and Biochemistry *20504
BC Hominidae 86215
IT Major Concepts
Behavior; Membranes (Cell Biology); Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
brain: histology, nervous system; cerebral cortex: nervous system; cytoskeleton; frontal cortex: nervous system; plasma membrane
IT Diseases
depression: behavioral and mental disorders; schizophrenia: behavioral and mental disorders
IT Chemicals & Biochemicals
G protein: distribution, membrane **protein**, mobility; **adenylyl cyclase**
IT Alternate Indexing
Depression (MeSH); Schizophrenia (MeSH)
IT Methods & Equipment
autopsy: evaluation method
IT Miscellaneous Descriptors
second messenger system; Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): cadaver, patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN **9012-42-4 (ADENYLYL CYCLASE)**

L114 ANSWER 5 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:297741 BIOSIS
DN PREV200100297741
TI Chronic treatment of C6 glioma cells with **antidepressant** drugs results in a redistribution of **Gsalpha**.
AU **Donati, Robert J.**; Thukral, Chandrashekhar; **Rasenick, Mark M. (1)**
CS (1) Department of Physiology and Biophysics, College of Medicine, University of Illinois at Chicago, 835 S. Wolcott Ave., Rm. E202, Chicago, IL, 60612-7342: raz@uic.edu USA
SO Molecular Pharmacology, (June, 2001) Vol. 59, No. 6, pp. 1426-1432. print. ISSN: 0026-895X.
DT Article
LA English
SL English
AB Previous studies have demonstrated that chronic treatment of C6 glioma cells with the **antidepressants** desipramine and fluoxetine increases the Triton X-100 solubility of the **G protein** **Gsalpha** (Toki et al., 1999). The **antidepressants** also caused a 50% decrease in the amount of **Gsalpha** localized to caveolae-enriched membrane domains. In this study, laser scanning confocal microscopy reveals that **Gsalpha** is localized to the plasma membrane as well as the cytosol in both treated and control cells. However, striking differences are seen in the distribution of **Gsalpha** in the long cellular processes after chronic treatment with these **antidepressant** drugs. Control cells display **Gsalpha** along the entire process with an especially high concentration of that **G protein** at the distal ends. Desipramine- or fluoxetine-treated cells show a more centralized clustering of **Gsalpha** in the Golgi region of the cell and a drastic reduction of **Gsalpha** in the cellular processes. There is no change in the distribution of **Goalpha** after desipramine treatment and the antipsychotic drug chlorpromazine does not alter **Gsalpha**. These results suggest that **antidepressant** -induced changes in the association of **Gsalpha** with the plasma membrane may translate into altered cellular localization of this signal transducing **protein**. Thus, modification of the coupling between **Gs**-coupled receptors and **adenylyl cyclase** may

underlie both **antidepressant** therapy and **depressive** illnesses. This report also suggests that modification of the membrane domain occupied by **Gsalpha** might represent a mechanism for chronic **antidepressant** effects.

CC Enzymes - General and Comparative Studies; Coenzymes *10802
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Biophysics - Membrane Phenomena *10508
Pathology, General and Miscellaneous - Therapy *12512
Nervous System - Physiology and Biochemistry *20504
Pharmacology - General *22002
Pharmacology - Psychopharmacology *22026

BC Muridae 86375

IT Major Concepts
Membranes (Cell Biology); Nervous System (Neural Coordination); Pharmacology

IT Parts, Structures, & Systems of Organisms
Golgi region; caveolae-enriched membrane domains; cellular processes; cytosol; plasma membrane

IT Diseases
depression: behavioral and mental disorders

IT Chemicals & Biochemicals
Gs-alpha: **G protein**, redistribution; **adenylyl cyclase**; **antidepressant** drugs; chlorpromazine: antipsychotic - drug; desipramine: **antidepressant** - drug; fluoxetine: **antidepressant** - drug

IT Alternate Indexing
Depression (MeSH)

IT Methods & Equipment
chronic drug treatment: therapeutic method; laser scanning confocal microscopy: microscopy method

IT Miscellaneous Descriptors
signal transduction

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
C6 cell line (Muridae): rat glioma cells

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

RN **9012-42-4 (ADENYLYL CYCLASE)**
50-53-3 (CHLORPROMAZINE)
50-47-5 (DESIPRAMINE)
54910-89-3 (FLUOXETINE)

L114 ANSWER 6 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:135070 BIOSIS
DN PREV200100135070
TI Serotonin induces MAPK activation in primary cultures of cortical neurons.
AU Tolbert, L. M. (1); Duman, R. S.
CS (1) Yale University, New Haven, CT USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-868.14. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT **Conference**
LA English
SL English
AB Although most classes of **antidepressants** act by increasing synaptic levels of serotonin and/or norepinephrine, the delayed therapeutic action of these drugs cannot by explained by their immediate effects. Two hypotheses have been proposed to explain the long-term changes in target neurons of serotonergic projections that may occur with long-term **antidepressant** treatment. Our lab has demonstrated

that chronic **antidepressant** administration upregulates several components of cAMP cascade, including the transcription factor CREB. Thus, CREB-mediated changes in gene expression could account for long-term adaptive changes underlying **antidepressant** action. Alternatively, the work of de Montigny et al. reveals that chronic **antidepressant** administration results in a progressive sensitization of post-synaptic 5-HT1A receptors, which are negatively coupled to **adenylyl cyclase** via the **G protein**, Gi. These seemingly contradictory findings can potentially be rationalized by the involvement of the MAPK cascade in 5-HT1A receptor signalling. Previous studies have shown that MAPK can induce CREB phosphorylation indirectly via the Rsk family of **protein** kinases. We have shown previously that serotonin and norepinephrine induce CREB phosphorylation in primary cultures of rat cortical neurons. Now we demonstrate that both 5-HT and NE induce MAPK phosphorylation with a similar time course. We have found that norepinephrine-induced MAPK activation is blocked by the **alpha1** antagonist prazosin, but is unaffected by the non-selective beta antagonist propranolol. We are currently investigating the contribution of the 5-HT1A receptor and other 5-HT receptor subtypes to MAPK activation using subtype-specific antagonists. Furthermore, we are studying the relationship between MAPK activation and CREB phosphorylation in order to elucidate the role of MAPK in CREB activation.

CC **Pharmacology - Psychopharmacology *22026**
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Cytology and Cytochemistry - Animal *02506
Behavioral Biology - General and Comparative Behavior *07002
Behavioral Biology - Animal Behavior *07003
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Pathology, General and Miscellaneous - Therapy *12512
Endocrine System - Neuroendocrinology *17020
Nervous System - Physiology and Biochemistry *20504
Pharmacology - General *22002

BC Muridae 86375

IT Major Concepts
Behavior; Nervous System (Neural Coordination); Pharmacology

IT Parts, Structures, & Systems of Organisms
cortical neuron: nervous system

IT Chemicals & Biochemicals
5-HT-1-A receptor; CREB: phosphorylation; MAPK: activation; **antidepressants: antidepressant**; norepinephrine; serotonin

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rat (Muridae)

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

RN 51-41-2 (NOREPINEPHRINE)
50-67-9 (SEROTONIN)

L114 ANSWER 7 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:131847 BIOSIS
DN PREV200100131847
TI Alterations in the detergent extraction of **G protein** from the plasma membrane from postmortem human brains of patients with **depression.**
AU Senda, S. (1); **Toki, S.**; Ozawa, H.; Choei, H.; Yamada, S.; Riederer, P.; Saito, T.
CS (1) Sapporo Medical Univ, Sapporo Japan
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract

No.-866.8. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience
. ISSN: 0190-5295.
DT **Conference**
LA English
SL English
AB Previous studies have suggested that attenuation of the **Gs** -mediated **adenylyl cyclase** (AC) activity in the cerebral cortex may be involved in the etiology of **depression**. Recently, it has been suggested that membrane **proteins** such as receptors, **G proteins** and effectors are associated with some cytoskeletal **proteins** that restrict the distribution and mobility of these **proteins** to a surprising degree. Furthermore, Toki et al. (1999) reported that the change in the distribution of **Gs alpha** in the plasma membrane caused by chronic **antidepressant** treatment affects the **G protein**-mediated AC activity. Therefore, in the present study, we examined the alteration in the distribution of **G proteins** in the plasma membrane from postmortem human brains of patients with **depression** and age-matched controls by the detergent extraction method. Tissue samples were obtained from nine unipolar **depressives** and nine controls. A membrane-enriched fraction was prepared from frontal cortex and stirred in ice-cold HEPES (15 muM, pH 7.4) containing 1% Triton X-100 (TX-100) for 60 min followed by centrifugation at 100,000 **g** for 60 min at 4degree C. The supernatant and pellet were collected and the amount of **Gs alpha** in each fraction was estimated by immunoblotting. TX-100 extracted less **Gs alpha** from the **depressive** group than from the control group and more **Gs alpha** remained in the pellet in the **depressive** group than in the control group. These data suggest that there is more **Gs alpha** in the strongly hydrophobic portion of the synaptic membrane in the **depressive** group than that in controls. Therefore, a change in the distribution of **G protein** may be involved in the etiology of **depression**.
CC Enzymes - General and Comparative Studies; Coenzymes *10802
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Behavioral Biology - Human Behavior *07004
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
BC Hominidae 86215
IT Major Concepts
Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
cerebral cortex: nervous system; plasma membrane
IT Diseases
depression: behavioral and mental disorders
IT Chemicals & Biochemicals
G protein; adenylyl cyclase
IT Alternate Indexing
Depression (MeSH)
IT Methods & Equipment
immunoblotting: analytical method; postmortem examination: analytical method
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN **9012-42-4 (ADENYLYL CYCLASE)**

L114 ANSWER 8 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:131846 BIOSIS
DN PREV200100131846
TI cAMP and inositol phosphates related signal transduction in **depressions** and schizophrenia.
AU Ozawa, H. (1); Yamaguchi, T.; Senda, S.; **Toki, S.**; Choiei, H.; Yamada, S.; Riederer, P.; Saito, T.
CS (1) Sapporo Medical University, Sapporo Japan
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-866.7. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT **Conference**
LA English
SL English
AB Mood disorders and schizophrenia are the two most important endogenous psychiatric diseases. Recently several researchers have suggested that there are common and overlapping symptoms between these two disorders., especially in terms of **depression** and negative symptoms of chronic schizophrenia. In the present study, we examined the productive activity of two second messengers systems (**adenylyl cyclase** (AC) which produces cAMP and phospholipase C (PLC) which produces Inositol phosphates (Ips)) in membrane preparations from postmortem frontal cortex of unipolar **depressive** patients without manic episodes.(11 patients AGE : 68.6+-3.5y, PMDT: 19.6+-10.1hr)and chronic schizophrenia (11 patients AGE : 67.3+-3.5y, PMDT: 10.8+-3.1hr) in comparison with control subjects (10 subjects AGE : 79.0 +-3.1y, PMDT: 10.0+- 3.58hr). Basal AC activity was significantly decreased in **depressives**, and Mn2+- **stimulated** AC activity had a tendency to decline compared to controls. In contrast to **depressions**, there were no differences in basal and Mn2+ **stimulated** AC activity between schizophrenia and controls. In the other hand, 5-HT-**stimulated** PLC activity was significantly increased in both **depressives** and schizophrenia compared to controls. These results indicated that the enhancement in 5HT2 receptor regulated IPs productions is related to the pathophysiology of both **depression** and chronic schizophrenia.
CC Enzymes - General and Comparative Studies; Coenzymes *10802
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Behavioral Biology - Human Behavior *07004
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Endocrine System - Neuroendocrinology *17020
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
BC Hominidae 86215
IT Major Concepts
Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
frontal cortex: nervous system
IT Diseases
depression: behavioral and mental disorders; manic episodes: behavioral and mental disorders, nervous system disease; mood disorder: behavioral and mental disorders, nervous system disease; schizophrenia: behavioral and mental disorders, negative symptoms, nervous system disease
IT Chemicals & Biochemicals
adenylyl cyclase; cyclic AMP; inositol phosphates; phospholipase C; serotonin; serotonin type II receptor

IT Alternate Indexing
Depression (MeSH); Mood Disorders (MeSH); Schizophrenia (MeSH)
IT Miscellaneous Descriptors
signal transduction; Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN **9012-42-4 (ADENYLYL CYCLASE)**
60-92-4 (CYCLIC AMP)
15421-51-9Q (INOSITOL PHOSPHATES)
68247-19-8Q (INOSITOL PHOSPHATES)
9001-86-9 (PHOSPHOLIPASE C)
50-67-9 (SEROTONIN)

L114 ANSWER 9 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:110540 BIOSIS
DN PREV200100110540
TI Chronic **antidepressant** treatment alters the cellular localization of **Gsalpha**.
AU **Donati, R. J. (1); Rasenick, M. M.**
CS (1) University of Illinois College of Medicine, Chicago, IL USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-387.15. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT **Conference**
LA English
SL English
AB Previous studies in this laboratory have demonstrated that **Gsalpha** from C6 rat glioma cells migrates from a Triton X-100 (TTX-100) insoluble membrane domain to a TTX-100 soluble membrane domain in response to chronic treatment with the **antidepressants** desipramine and fluoxetine (Toki et al., 1999 J. Neurochem. 73(3): 1114-1120). In this same study it was also reported that there was a 50% decrease in the amount of **Gsalpha** localized to caveolae-enriched TTX-100 insoluble membranes. Current studies have focused on visualizing this pattern of **Gsalpha** movement using laser scanning confocal microscopy. **Gsalpha** is localized to the plasma membrane as well as the cytosol in both the treated and control cells. However, striking differences are seen in the distribution of **Gsalpha** in the long cellular processes. Control cells express **Gsalpha** along the entire process with a high concentration at the distal end while desipramine treated cells show a more centralized clustering of **Gsalpha** in the Golgi region of the cell. Furthermore, the appearance of **Gsalpha** in the processes is drastically reduced in the treated cells. There is no change in the distribution of Goalpha after desipramine treatment. Fluoxetine also induces the transfer of **Gsalpha**, however the number of cells observed with this pattern of relocation is fewer than that seen with desipramine. These results suggest that **antidepressant**-induced changes in the association of **Gsalpha** with the plasma membrane may translate into altered cellular localization of this signal transducing protein.
CC Pharmacology - General *22002
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Cytology and Cytochemistry - General *02502
Cytology and Cytochemistry - Animal *02506
Behavioral Biology - General and Comparative Behavior *07002
Behavioral Biology - Animal Behavior *07003
Biochemical Studies - General *10060
Pathology, General and Miscellaneous - Therapy *12512

Nervous System - Physiology and Biochemistry *20504
Pharmacology - Psychopharmacology *22026
BC Muridae 86375
IT Major Concepts
Behavior; Cell Biology; Nervous System (Neural Coordination); Pharmacology
IT Parts, Structures, & Systems of Organisms
cytosol; plasma membrane
IT Chemicals & Biochemicals
Gs-alpha: cellular localization alteration, signal transducing protein; Triton X-100 insoluble membranes; desipramine: **antidepressant** - drug, chronic treatment; fluoxetine: **antidepressant** - drug, chronic treatment
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
C6 cell line (Muridae): rat glioma cells
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 50-47-5 (DESIPRAMINE)
54910-89-3 (FLUOXETINE)

L114 ANSWER 10 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:83580 BIOSIS
DN PREV200000083580
TI Both the membrane association and cellular localization of **Gsalpha** are altered by **antidepressant** treatment.
AU **Donati, Robert J. (1); Rasenick, Mark M. (1)**
CS (1) University of Illinois at Chicago, 835 S. Wolcott, Chicago, IL, 60612 USA
SO Molecular Biology of the Cell, (Nov., 1999) Vol. 10, No. SUPPL., pp. 419a. Meeting Info.: 39th Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 11-15, 1999 The American Society for Cell Biology
. ISSN: 1059-1524.
DT **Conference**
LA English
CC Biophysics - Membrane Phenomena *10508
Cytology and Cytochemistry - Animal *02506
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Muridae 86375
IT Major Concepts
Membranes (Cell Biology)
IT Parts, Structures, & Systems of Organisms
membrane
IT Chemicals & Biochemicals
G-s-**alpha**: localization; Triton X-100; **antidepressants**; caveolin
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
C6 cell line (Muridae): rat glioma cells
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 9002-93-1 (TRITON X-100)

L114 ANSWER 11 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:451149 BIOSIS
DN PREV199900451149

TI Treatment of C6 glioma cells and rats with **antidepressant** drugs increases the detergent extraction of **Gsalpha** from plasma membrane.

AU **Toki, Sadamu; Donati, Robert J.; Rasenick, Mark M. (1)**
CS (1) Department of Physiology and Biophysics, University of Illinois College of Medicine, 835 S. Wolcott Avenue, Chicago, IL, 60612-7342 USA

SO Journal of Neurochemistry, (Sept., 1999) Vol. 73, No. 3, pp. 1114-1120. ISSN: 0022-3042.
DT Article
LA English
SL English

AB Results from previous studies suggested that chronic treatment of rats or C6 glioma cells with **antidepressants** augments the coupling between **Gs** and **adenylyl cyclase**. As these effects on C6 glioma cells are seen in the absence of presynaptic input, several **antidepressant** drugs may have a direct "postsynaptic" effect on their target cells. It was hypothesized that the target of **antidepressant** action was some membrane **protein** that may regulate coupling between **G proteins** and **adenylyl cyclase**. To test this, C6 glioma cells were treated with amitriptyline, desipramine, iprindole, or fluoxetine for 3 days. Chlorpromazine served as a control for these treatments. Membrane **proteins** were extracted sequentially with Triton X-100 and Triton X-114 from C6 glioma cells. Triton X-100 extracted more **Gsalpha** in membranes prepared from **antidepressant**-treated C6 glioma cells than from control groups. In addition, cell fractionation studies revealed that the amount of **Gsalpha** in caveolin-enriched domainswas reduced after **antidepressant** treatment and that **adenylyl cyclase** comigrated with **Gsalpha** in the gradients. These data suggest that some postsynaptic component that increases availability of **Gs** to activate effector molecules, such as **adenylyl cyclase**, might be a target of **antidepressant** treatment.

CC Pharmacology - General *22002
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Biophysics - Membrane Phenomena *10508
Enzymes - General and Comparative Studies; Coenzymes *10802
Metabolism - General Metabolism; Metabolic Pathways *13002
Nervous System - General; Methods *20501
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
BC Muridae 86375
IT Major Concepts
Cell Biology; Nervous System (Neural Coordination); Pharmacology
IT Parts, Structures, & Systems of Organisms
plasma membrane: blood and lymphatics
IT Chemicals & Biochemicals
adenylyl cyclase; amitriptyline: **antidepressant** - drug; chlorpromazine: **antidepressant** - drug; desipramine: **antidepressant** - drug; fluoxetine: **antidepressant** - drug; iprindole: **antidepressant** - drug; **G protein**; **G-s alpha**: detergent extraction
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae); C6 cell line (Muridae): rat glioma cells
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN **9012-42-4 (ADENYLYL CYCLASE)**
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)
5560-72-5 (IPRINDOLE)
54910-89-3 (FLUOXETINE)

50-53-3 (CHLORPROMAZINE)

L114 ANSWER 12 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:447949 BIOSIS
DN PREV199900447949
TI **G protein**-coupled cyclic AMP signaling in postmortem brain of subjects with mood disorders: Effects of diagnosis, suicide, and treatment at the time of death.
AU Dowlatshahi, Dar; MacQueen, Glenda M.; Wang, Jun-Feng; Reiach, James S.; Young, L. Trevor (1)
CS (1) Department of Psychiatry and Behavioural Neurosciences, McMaster University, HSC-4N77A, 1200 Main St. W., Hamilton, ON, L8N 3ZS Canada
SO Journal of Neurochemistry, (Sept., 1999) Vol. 73, No. 3, pp. 1121-1126. ISSN: 0022-3042.
DT Article
LA English
SL English
AB Components of cyclic AMP (cAMP) signaling were examined in postmortem cerebral cortex of a well characterized group of patients with mood disorders and nonpsychiatric control subjects. We measured **G protein** levels, **adenylyl cyclase** (AC) activity, and CREB levels in cerebral cortex of the subjects with respect to diagnosis, treatment, and suicide. There was no effect of diagnosis on any measure, except for a trend toward decreased **stimulated** AC activity in subjects with mood disorders relative to control subjects. We also detected a significant effect of suicide on temporal cortex CREB levels in subjects that died as a result of suicide relative to those that did not, which was more evident in patients with major **depressive** disorder. Bipolar disorder (BD) subjects treated with anticonvulsants at the time of death had decreased temporal cortex CREB levels relative to those not receiving anticonvulsants. Furthermore, we found a trend toward decreased occipital cortex **Galphas** (short) levelsin BD subjects treated with lithium. These results support the hypothesis of altered cAMP signaling in mood disorders and raise the possibility that factors other than diagnosis, such as treatment and suicide, may be relevant to cell-signaling abnormalities reported in the literature.
CC Nervous System - General; Methods *20501
Biochemical Studies - General *10060
Enzymes - General and Comparative Studies; Coenzymes *10802
Pathology, General and Miscellaneous - Diagnostic *12504
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - General Metabolism; Metabolic Pathways *13002
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
brain: nervous system, postmortem; cerebral cortex: nervous system; occipital cortex: nervous system
IT Diseases
bipolar disorder: behavioral and mental disorders; mood disorder: behavioral and mental disorders, treatment, diagnosis; suicide: behavioral and mental disorders
IT Chemicals & Biochemicals
adenylyl cyclase: activity; cyclic AMP: signaling; CREB [cyclic AMP-response element binding **protein**]; **G protein; G protein**-coupled cyclic AMP: signaling
IT Alternate Indexing
Bipolar Disorder (MeSH); Mood Disorders (MeSH); Suicide (MeSH)
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 60-92-4 (CYCLIC AMP)
9012-42-4 (ADENYLYL CYCLASE)

L114 ANSWER 13 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:80153 BIOSIS
DN PREV199900080153
TI Modification of the interaction between **G protein** and the cytoskeleton after chronic **antidepressant** treatment.
AU **Toki, S.; Rasenick, M. M.**
CS Dep. Physiol. Biophysics, Univ. Ill. Coll. Med., Chicago, IL 60612 USA
SO Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 1490.
Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part 2 Los Angeles, California, USA November 7-12, 1998
ISSN: 0190-5295.
DT **Conference**
LA English
CC Nervous System - General; Methods *20501
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Pharmacology - General *22002
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Muridae 86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination); Pharmacology
IT Parts, Structures, & Systems of Organisms
cytoskeleton; presynaptic membranes
IT Chemicals & Biochemicals
adenylyl cyclase; amitriptyline: **antidepressant** - drug; fluoxetine: **antidepressant** - drug; iprindole: **antidepressant** - drug; **G protein**
IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae); C6 cell line (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN **9012-42-4 (ADENYLYL CYCLASE)**
50-48-6 (AMITRIPTYLINE)
54910-89-3 (FLUOXETINE)
5560-72-5 (IPRINDOLE)

L114 ANSWER 14 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:533807 BIOSIS
DN PREV199799833010
TI Chronic **antidepressant** treatment alters the interaction between **G proteins** and the cytoskeleton.
AU **Toki, S.; Rasenick, M. M.**
CS Dep. Physiol. Biophysics, Univ. Ill. Coll. Med., Chicago, IL 60612 USA
SO Society for Neuroscience Abstracts, (1997) Vol. 23, No. 1-2, pp. 2232.
Meeting Info.: 27th Annual Meeting of the Society for Neuroscience New Orleans, Louisiana, USA October 25-30, 1997
ISSN: 0190-5295.
DT **Conference**; Abstract; **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Enzymes - General and Comparative Studies; Coenzymes *10802

Nervous System - General; Methods *20501
Pharmacology - General *22002
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Nervous System (Neural Coordination); Pharmacology
IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; IMIPRAMINE; IPRINDOLE
IT Miscellaneous Descriptors
ADENYLYL CYCLASE; AMITRIPTYLINE; **ANTIDEPRESSANT**-DRUG; **ANTIDEPRESSANTS**; CHRONIC **ANTIDEPRESSANT** TREATMENT; CYTOSKELETON; EXPERIMENTAL METHOD; **G PROTEIN**; IMIPRAMINE; IPRINDOLE; MEMBRANES; NERVOUS SYSTEM; PHARMACOLOGY; POST-SYNAPTIC EFFECT; SYNAPTIC MEMBRANES
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9012-42-4** (**ADENYLYL CYCLASE**)
50-48-6 (AMITRIPTYLINE)
50-49-7 (IMIPRAMINE)
5560-72-5 (IPRINDOLE)

L114 ANSWER 15 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:125196 BIOSIS
DN PREV199799431699
TI Genetic markers of alcohol abuse.
AU Ferguson, Ralph A.; Goldberg, David M. (1)
CS (1) Dep. Clinical Biochemistry, Banting Inst., Univ. Toronto, 100 Banting Street, Toronto, ON M5G 1L5 Canada
SO Clinica Chimica Acta, (1997) Vol. 257, No. 2, pp. 199-250.
ISSN: 0009-8981.
DT General Review
LA English
AB In this paper, we review the current status of genetic markers for the development of alcohol abuse. Family, twin, half-sibling and adoption studies of alcoholic subjects suggest that the heritability of liability to alcoholism is at least 50%. These findings have fuelled intensive investigation in the fields of neurology, biochemistry, genetics and molecular biology aimed at the identification of markers for the risk of alcoholism. The most promising of these are discussed in detail. Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) polymorphisms, specifically the ADH3*1, ADH2*2, and ALDH2*2 genotypes appear to confer a protective effect against alcoholism, most notably in Oriental subjects. Caucasian alcohol abusers and their first-degree relatives exhibit **depressed** platelet monoamine oxidase activity, the degree of which is greater in Type II than Type I alcoholics. Electrophysiological characteristics of alcoholics and those at risk for developing alcoholism have also been identified, including the reduced amplitude of the event-related brain potential and, after ethanol ingestion, characteristic EEG **alpha**-wave activity. Lower platelet **adenylate cyclase** activity is seen in alcoholics compared to controls, presumably as a result of over-expression of an inhibitory **G-protein**. Markers related to other signal transduction pathways of the central nervous system including the serotoninergic, muscarinic and dopaminergic systems are also discussed. In this group of markers, the putative association between the inheritance of the A1 allele of the D2 dopamine receptor and the susceptibility to alcoholism provides the most dramatic illustration of the challenges presently existing in this field of scientific investigation. Current limitations in the definition, diagnosis and classification of alcoholism, the confounding influences of

race and gender on association studies, as well as the statistical approach of linkage studies are discussed as they relate to the endeavor to uncover valid genetic markers for the risk of alcoholism.

CC Genetics and Cytogenetics - Human *03508
Genetics and Cytogenetics - Sex Differences *03510
Social Biology; Human Ecology *05500
Behavioral Biology - Human Behavior 07004
Enzymes - Physiological Studies *10808
Psychiatry - Addiction - Alcohol, Drugs, Smoking, etc. *21004
Toxicology - General; Methods and Experimental *22501

BC Hominidae *86215

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Genetics; Human Ecology (Anthropology); Psychiatry (Human Medicine, Medical Sciences); Toxicology

IT Chemicals & Biochemicals
ALCOHOL; ALCOHOL DEHYDROGENASE; ALDEHYDE DEHYDROGENASE

IT Miscellaneous Descriptors
ALCOHOL ABUSE; ALCOHOL DEHYDROGENASE; ALDEHYDE DEHYDROGENASE; BEHAVIOR; BEHAVIORAL AND MENTAL DISORDERS; ETHNIC DIFFERENCES; GENDER DIFFERENCES; GENETIC MARKERS; TOXICOLOGY

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN 64-17-5 (ALCOHOL)
9031-72-5 (ALCOHOL DEHYDROGENASE)
9028-86-8 (ALDEHYDE DEHYDROGENASE)

L114 ANSWER 16 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:33767 BIOSIS
DN PREV199799340170
TI Regulation of signal transduction pathways by mood-stabilizing agents: Implications for the delayed onset of therapeutic efficacy.
AU Manji, Husseini K. (1); Chen, Guang; Hsiao, John K.; Risby, Emile D.; Masana, Monica I.; Potter, William Z.
CS (1) Schizophrenia Mood Disorders Clin. Res. Div., Dep. Psychiatr. Behavioral Neurosci., Wayne State Univ. Sch. Med., UHC 9B, 4201 St. Antoine Blvd., Detroit, MI 48201 USA
SO Journal of Clinical Psychiatry, (1996) Vol. 57, No. SUPPL. 13, pp. 34-46. ISSN: 0160-6689.
DT General Review
LA English
AB A series of investigations were performed to elucidate the mechanisms of action of lithium, valproate, and carbamazepine. We have found that lithium exerts major effects on **G proteins**, most likely via a posttranslational process stabilizing the inactive heterotrimeric (**alpha**-beta-gamma) form of the **protein**. We also find that chronic lithium and valproate exert major, very similar effects on the PKC signaling pathway, with both drugs decreasing the levels of membrane-associated PKC **alpha** and epsilon, and have similar effects on the DNA binding activity of the transcription factor, AP-1. By contrast, we find that carbamazepine exerts major, direct inhibitory effect at the level of **adenylyl cyclases**. Overall, the results suggest that signal transduction pathways are targets for the actions of mood-stabilizing agents; given their key roles in the amplification and integration of signals in the central nervous system, these findings have clear implications not only for research into the etiology/pathophysiology of manic-**depressive** illness, but also for the development of innovative treatment strategies.
CC Cytology and Cytochemistry - Animal *02506
Behavioral Biology - Human Behavior *07004
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy *12512
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
BC Hominidae *86215
IT Major Concepts
Behavior; Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Pathology; Pharmacology; Psychiatry (Human Medicine, Medical Sciences)
IT Chemicals & Biochemicals
LITHIUM; VALPROATE; CARBAMAZEPINE; PROTEIN KINASE C
IT Miscellaneous Descriptors
ANTIDEPRESSANT AGENTS; **ANTIDEPRESSANT**-DRUG; BEHAVIOR; BEHAVIORAL AND MENTAL DISORDERS; CARBAMAZEPINE; DELAYED ONSET; DELAYED ONSET OF ACTION; **G PROTEIN**; LITHIUM; MANIA; MOOD-STABILIZING AGENTS; PHARMACODYNAMICS; PHARMACOLOGY; **PROTEIN** KINASE C; SIGNAL TRANSDUCTION PATHWAY REGULATION; THERAPEUTIC EFFICACY; TREATMENT; VALPROATE
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 7439-93-2 (LITHIUM)
99-66-1 (VALPROATE)
298-46-4 (CARBAMAZEPINE)
141436-78-4 (PROTEIN KINASE C)

L114 ANSWER 17 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:23283 BIOSIS
DN PREV199799322486
TI Beta-Adrenoceptor-linked protein kinase A (PKA) activity in human fibroblasts from normal subjects and from patients with major **depression.**
AU Manier, D. Hal; Eiring, Andrea; Shelton, Richard C.; Sulser, Fridolin (1)
CS (1) Vanderbilt Univ. Sch. Med., AA-2232 MCN, Nashville, TN 37232 USA
SO Neuropsychopharmacology, (1996) Vol. 15, No. 6, pp. 555-561.
ISSN: 0893-133X.
DT Article
LA English
AB Human fibroblasts from normal subjects and from patients with major **depression** are cultured and their beta-adrenoreceptor-cyclic AMP-**protein** kinase A (PKA) system characterized. The results indicate that the beta-adrenoreceptor-mediated activation of PKA in the 900 **g** supernatant fraction of human fibroblasts is mediated via beta-adrenoreceptors. The activation of PKA by isoproterenol is very rapid with maximal **stimulation** occurring at 5 seconds. The time course of PKA activation by isoproterenol in fibroblasts from patients with major **depression** is identical to that in fibroblasts from normal subjects but the magnitude of activation is significantly reduced in fibroblasts from patients with major **depression**. Dose-response curves on cyclic AMP mediated activation of PKA confirmed the previously reported reduction in activation of PKA in patients with major **depression** but demonstrated that this reduction occurs without a change in the EC-50 values of cyclic AMP (approximately 20 nmol/L). The blunted beta-adrenoceptor-linked PKA responses in patients with major **depression** occur without a change in the expression of the PKA catalytic subunit C-**alpha**. The studies suggest that the beta-adrenoceptor-coupled **adenylate cyclase** PKA system in human fibroblasts may represent a valid model to explore possible abnormalities in the fine tuning of the beta-adrenergic transduction cascade in patients with affective disorders.
CC Cytology and Cytochemistry - Human *02508

Behavioral Biology - Human Behavior *07004
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
BC Hominidae *86215
IT Major Concepts
Behavior; Biochemistry and Molecular Biophysics; Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences)
IT Chemicals & Biochemicals
PROTEIN KINASE A; ISOPROTERENOL
IT Miscellaneous Descriptors
ACTIVITY; BETA-ADRENERGIC TRANSDUCTION CASCADE; BETA-ADRENOCEPTOR; BETA-ADRENOCEPTOR-CYCLIC AMP-PROTEIN KINASE A; FIBROBLAST; ISOPROTERENOL; MAJOR **DEPRESSION**; NEUROLOGY; PATIENT
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 142008-29-5 (PROTEIN KINASE A)
7683-59-2 (ISOPROTERENOL)

L114 ANSWER 18 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:467852 BIOSIS
DN PREV199699190208
TI Lack of effect of chronic **antidepressant** treatment on **Gs** and Gi **alpha**-subunit protein and mRNA levels in the rat cerebral cortex.
AU Emamghoreishi, Masoumeh; Warsh, Jerry J.; Sibony, David; Li, Peter P. (1)
CS (1) Sect. Biochem. Psychiatry, Clarke Inst. Psychiatry, 250 College St., Toronto, ON M5T 1R8 Canada
SO Neuropsychopharmacology, (1996) Vol. 15, No. 3, pp. 281-287. ISSN: 0893-133X.
DT Article
LA English
AB Experimental evidence indicates that chronic **antidepressant** treatment in rats modifies the central nervous system beta-adrenoceptor signaling pathway at multiple sites including receptor, **G-protein, adenylyl cyclase,** and **protein** kinase A. In the present study, we examined the postreceptor effect of **antidepressant** treatment on the **protein** and mRNA levels of **stimulatory** and inhibitory **G protein** **alpha**-subunits (**G-alpha**-s and **G-alpha**-i) and beta-subunits in rats infused continuously with various **antidepressants** for 21 days. Chronic treatment with tricyclic (desipramine and amitriptyline) and monoamine oxidase inhibiting (tranylcypromine) **antidepressants** did not significantly affect the immunoreactivity levels of **G-alpha**-s (both 45- and 52-kDa species), **G-alpha**-i1, Ga-i2, **G** -beta-36, and beta-35 in rat cerebral cortex. Similarly, the levels of mRNA encoding these **G protein** subunits remained unchanged subsequent to these drug treatments. In contrast, cortical beta-adrenoceptor number was significantly decreased by these treatments. These results suggest that the adaptive changes of rat cerebral cortical beta-adrenoceptor-**adenylyl cyclase** system often seen after chronic **antidepressant** treatment are not accompanied by changes in the abundance and gene expression of **G-alpha** -s, **G-alpha**-i, or **G**-beta **proteins**.
CC Cytology and Cytochemistry - Animal *02506

Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Endocrine System - Neuroendocrinology *17020
Nervous System - Physiology and Biochemistry *20504
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026

BC Muridae *86375

IT Major Concepts
Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Nervous System (Neural Coordination); Pharmacology

IT Chemicals & Biochemicals
ADENYLYL CYCLASE; PROTEIN KINASE A; DESIPRAMINE; AMITRIPTYLINE; TRANYLCYPROMINE; MONOAMINE OXIDASE

IT Miscellaneous Descriptors
ADENYLYL CYCLASE; AMITRIPTYLINE; **ANTIDEPRESSANT**-DRUG; BETA-ADRENOCEPTOR; CEREBRAL CORTEX; CHRONIC **ANTIDEPRESSANT** TREATMENT; DESIPRAMINE; ENZYME INHIBITOR-DRUG; **G-PROTEIN**; GI **ALPHA** -SUBUNIT **PROTEIN**; **GS ALPHA**-SUBUNIT **PROTEIN**; MESSENGER RNA; MONOAMINE OXIDASE; MRNA; NERVOUS SYSTEM; PHARMACOLOGY; **PROTEIN** KINASE A; SIGNAL TRANSDUCTION; THERAPEUTIC METHOD; TRANYLCYPROMINE

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rat (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

RN **9012-42-4** (**ADENYLYL CYCLASE**)
142008-29-5 (PROTEIN KINASE A)
50-47-5 (DESIPRAMINE)
50-48-6 (AMITRIPTYLINE)
155-09-9 (TRANYLCYPROMINE)
9001-66-5 (MONOAMINE OXIDASE)

L114 ANSWER 19 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:427050 BIOSIS
DN PREV199699158106
TI Lack of effect of **antidepressants** on mononuclear leukocyte **G-protein** levels or function in **depressed** outpatients.
AU Young, L. Trevor (1); Li, Peter P.; Kamble, Arvind; Siu, Kin Po; Warsh, Jerry J.
CS (1) Dep. Psychiatry, Fac. Health Sci., McMaster Univ., 1200 Main St. W., Hamilton, ON L8N 3Z5 Canada
SO Journal of Affective Disorders, (1996) Vol. 39, No. 3, pp. 201-207. ISSN: 0165-0327.
DT Article
LA English
AB Evidence from studies in animal and cultured cell models suggests that **antidepressants** (ADs) may enhance postreceptor signalling through the **G protein** coupled **adenylyl cyclase** (AC) pathways. To test whether this also occurs in patients receiving AD treatment, **G-protein** -activated-AC activity and the levels of **alpha**-s and **alpha**-i were measured in mononuclear leukocytes (MNLs) from 12 subjects with major **depressive** disorder (MDD) at baseline and after a 5 week trial of AD treatment. Although no differences were found in GTP-gamma-S-and forskolin-**stimulated** AC activity or the levels of **alpha**-s and **alpha**-i in MDD subjects compared with age- and sex-matched healthy subjects, pretreatment basal AC activity

was significantly lower in treatment responders compared with healthy subjects. No significant changes were evident in any of these biochemical measures following 5 weeks of AD treatment in the patient group as a whole or stratified by response. These findings do not support an effect of ADs on the **G-protein** AC pathway, at least in MNLs. Lower pretreatment basal AC activity in responders suggests some change(s) in post-receptor signalling processes may be associated with an increased likelihood of therapeutic response to ADs.

CC Behavioral Biology - Human Behavior 07004
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Psychopharmacology *22026

BC Hominidae *86215

IT Major Concepts
Pharmacology; Psychiatry (Human Medicine, Medical Sciences)

IT Chemicals & Biochemicals
ADENYLYL CYCLASE; CYCLASE

IT Miscellaneous Descriptors
ADENYLYL CYCLASE; ANTIDEPRESSANT THERAPY; BEHAVIORAL AND MENTAL DISORDERS; ENZYME SUBSTRATE; **G-PROTEIN; G-PROTEIN**-ACTIVATED-**ADENYLYL CYCLASE** PATHWAY; MAJOR **DEPRESSIVE** DISORDER; MONONUCLEAR LEUKOCYTE; PATIENT; PHARMACOKINETICS; PHARMACOLOGY; SECOND MESSENGER; THERAPEUTIC METHOD; THERAPEUTIC RESPONSE

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN **9012-42-4** (**ADENYLYL CYCLASE**)
9074-90-2 (**CYCLASE**)

L114 ANSWER 20 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:233860 BIOSIS
DN PREV199698797989
TI Platelet phosphoinositide signaling system: An overstimulated pathway in **depression.**
AU Karege, Felicien (1); Bovier, Philippe; Rudolph, Waltraut; Gaillard, Jean-Michel
CS (1) Univ. Geneva Inst. Neuropsychiatry, 2 ch. Petit Bel-Air, CH-1225 Chene-Bourg, Geneva Switzerland
SO Biological Psychiatry, (1996) Vol. 39, No. 8, pp. 697-702. ISSN: 0006-3223.
DT Article
LA English
AB In order to test a possible **depression**-associated defect in signal transduction, platelet **alpha2**-adrenergic-mediated phosphoinositide (PI) hydrolysis was measured, both in drug-free major **depressed** patients and in control healthy subjects. Results that express phospholipase C activity have shown significant increase in the metabolites of epinephrine-**stimulated** tritiated phosphatidyl-4,5-biphosphate (3H-PIP-2) with respect to basal activity (salinestimulated). Thrombin (2 units) and 10 mM sodium fluoride (NaF) also induced an increase in 3H-PIP-2 metabolites. These increases were potentiated in drug-free **depressed** patients both in epinephrine-and thrombin-**stimulated** platelets. In contrast, sodium fluoride, which directly **stimulates G protein** without receptor interaction, did not differentiate between patients and controls with respect to PI hydrolysis. This result suggests a possible **depression**-associated defect in heterologous receptor-**G protein** interaction.
CC Cytology and Cytochemistry - Human 02508
Behavioral Biology - Human Behavior 07004
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biochemical Studies - Lipids 10066
Biochemical Studies - Minerals 10069
Enzymes - Physiological Studies *10808
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Endocrine System - Neuroendocrinology *17020
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
BC Hominidae *86215
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences)
IT Chemicals & Biochemicals
EPINEPHRINE; THROMBIN; SODIUM; PHOSPHOLIPASE C; **ADENYLATE CYCLASE**
IT Miscellaneous Descriptors
ADENYLATE CYCLASE; EPINEPHRINE; PHOSPHATIDYL-4,5-BIPHOSPHATE; PHOSPHOLIPASE C; SIGNAL TRANSDUCTION; SODIUM CHLORIDE; THROMBIN; 1,2-DIACYLGLYCEROL; 1,4,5-TRIPHOSPHATE
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 51-43-4 (EPINEPHRINE)
9002-04-4 (THROMBIN)
7440-23-5 (SODIUM)
9001-86-9 (PHOSPHOLIPASE C)
9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 21 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:554266 BIOSIS
DN PREV199698568566
TI Chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content.
AU Chen, Jiang; **Rasenick, Mark M. (1)**
CS (1) Dep. Physiol. Biophysics, Univ. Illinois Coll. Medicine, 901 S. Wolcott Ave., Chicago, IL 60612-7342 USA
SO Journal of Pharmacology and Experimental Therapeutics, (1995) Vol. 275, No. 1, pp. 509-517.
ISSN: 0022-3565.
DT Article
LA English
AB It has been suggested that the molecular basis of **antidepressant** action involves postreceptor components. Results from our studies have suggested that a **G protein** (**G**-s) is one of those targets and that chronic **antidepressant** treatment facilitates the activation of **adenylyl cyclase** by **G-salpha**. This report represents an attempt to define which aspects of **G protein** function are altered by chronic **antidepressant** treatment. Rats were treated for 21 days with amitriptyline, desipramine, ABT 200 (a pyrollidine with putative **antidepressant** effects) or electroconvulsive shock, and membranes were prepared from the cerebral cortexes. Each of these treatments caused an increase in membrane **adenylyl cyclase** assayed in the presence of guanyl-5'imidodiphosphate (gtoreq 1 mu-M). Results of acute **antidepressant** treatments were no different than those of control treatment. Chronic treatment with amphetamine, which inhibits neurotransmitter reuptake without displaying **antidepressant** effect, was also ineffective in increasing **G-salpha stimulation** of **adenylyl cyclase**. Chronic **antidepressant** treatment did not change the content of **G protein**, as no change at the level of **G-salpha**

, **G-ialpha, G-oalpha** or **G**
-beta **protein** was detected by immunoblotting. Although there was
no change in the amount of **G proteins,**
antidepressant treatment increased the number of active **G**
-salpha/adenylyl cyclase complexes
immunoprecipitated by an anti-**G-salpha** antibody. It is
suggested that chronic **antidepressant** treatment alters certain
membrane components such that a greater proportion of **G-**
salpha is activated, **G-salpha** enjoys a more
fruitful interaction with **adenylyl cyclase,** or both.

CC Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Proteins, Peptides and Amino Acids *13012
Nervous System - Physiology and Biochemistry *20504
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Clinical Pharmacology 22005
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026

BC Muridae *86375

IT Major Concepts
Behavior; Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Nervous System (Neural Coordination); Pathology; Pharmacology

IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE

IT Miscellaneous Descriptors
ABT 200; AMITRIPTYLINE; **ANTIDEPRESSANT**-DRUG; DESIPRAMINE; MOLECULAR ACTIVITY; PHARMACODYNAMICS

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rat (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

RN **9012-42-4 (ADENYLYL CYCLASE)**
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)

L114 ANSWER 22 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:516658 BIOSIS
DN PREV199598530958
TI Chronic **antidepressant** treatment increases coupling between the **G protein, Gs** and **type VI adenylyl cyclase.**
AU Chen, J.; Chaney, K.; **Rasenick, M. M.**
CS Dep. Physiol. Biophysics, Univ. Ill. Coll. Med., Chicago, IL 60612 USA
SO Society for Neuroscience Abstracts, (1995) Vol. 21, No. 1-3, pp. 1865.
Meeting Info.: 25th Annual Meeting of the Society for Neuroscience San Diego, California, USA November 11-16, 1995
ISSN: 0190-5295.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Membrane Phenomena *10508
External Effects - Electric, Magnetic and Gravitational Phenomena 10610
Enzymes - Physiological Studies *10808
Nervous System - Physiology and Biochemistry *20504
Pharmacology - Neuropharmacology *22024

Pharmacology - Psychopharmacology *22026
BC Muridae *86375
IT Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Nervous System (Neural Coordination); Pharmacology
IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE; AMPHETAMINE
IT Miscellaneous Descriptors
AMITRIPTYLINE; AMPHETAMINE; **ANTIDEPRESSANT**-DRUG; DESIPRAMINE; ELECTROCONVULSIVE SHOCK; MEETING ABSTRACT; MEETING POSTER; SIGNAL TRANSDUCTION
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9012-42-4 (ADENYLYL CYCLASE)**
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)
300-62-9 (AMPHETAMINE)

L114 ANSWER 23 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:515202 BIOSIS
DN PREV199598529502
TI Participation of vitamin B-12 in beta-receptor mediated regulation of **adenylyl cyclase** system.
AU Watanabe, M. (1); Hatta, S.; Ikeda, H. (1); **Toki, S. (1)**; Ozawa, H. (1); Saito, T. (1); Takahata, N. (1)
CS (1) Dep. Neuropsyhciatry, Sch. Med., Sapporo Med. Univ., Sapporo 060 Japan
SO Society for Neuroscience Abstracts, (1995) Vol. 21, No. 1-3, pp. 1614. Meeting Info.: 25th Annual Meeting of the Society for Neuroscience San Diego, California, USA November 11-16, 1995
ISSN: 0190-5295.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - Vitamins 10063
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Metabolism - Water-Soluble Vitamins *13018
Nutrition - Malnutrition; Obesity *13203
Nutrition - Water-Soluble Vitamins *13210
Endocrine System - Neuroendocrinology *17020
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
BC Hominidae 86215
Muridae *86375
IT Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Metabolism; Neurology (Human Medicine, Medical Sciences); Nutrition; Psychiatry (Human Medicine, Medical Sciences)
IT Chemicals & Biochemicals
VITAMIN B12; **ADENYLYL CYCLASE**; MECOBALAMIN; S-ADENOSYL-L-METHIONINE
IT Miscellaneous Descriptors
ALZHEIMER'S DISEASE; BETA-ADRENERGIC RECEPTOR; CLINICAL IMPLICATIONS; DEMENTIA; **DEPRESSION**; HUMAN MODEL; MECOBALAMIN; MEETING ABSTRACT; MEETING POSTER; S-ADENOSYL-L-METHIONINE; SCHIZOPHRENIA;

SIGNAL TRANSDUCTION CASCADE; VITAMIN B12 DEFICIENCY
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae); Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates
RN 68-19-9 (VITAMIN B12)
9012-42-4 (ADENYLYL CYCLASE)
13422-55-4 (MECOBALAMIN)
29908-03-0 (S-ADENOSYL-L-METHIONINE)

L114 ANSWER 24 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:161987 BIOSIS
DN PREV199598176287
TI Guanine nucleotide-binding proteins in bipolar affective disorder: Effects of long-term lithium treatment.
AU Manji, Husseini K. (1); Chen, Guang; Shimon, Hady; Hsiao, John K.; Potter, William Z.; Belmaker, Robert H.
CS (1) Sect. Clin. Pharmacol., NIMH, Build. 10, Room 2D46, 9000 Rockville Pk., Bethesda, MD 20892 USA
SO Archives of General Psychiatry, (1995) Vol. 52, No. 2, pp. 135-144. ISSN: 0003-990X.
DT Article
LA English
AB Background: This study examines recent suggestions from a number of investigators that signal-transducing guanine nucleotide-binding (**G**) **proteins** may be involved in the pathophysiology of bipolar affective disorder and may represent molecular targets for lithium's mood-stabilizing actions. Methods: We used selective antibodies to quantitate the levels of the **G protein alpha** subunits that regulate **adenylate cyclase** activity (**G-alpha**-s and **G-alpha** -i2) and phosphoinositide turnover (**G-alpha**-q/11). We also quantitated levels of pertussis toxin-catalyzed phosphate 32-labeled adenosine diphosphate ((32P)ADP) ribosylation in platelet and leukocyte membranes from a group of 14 untreated (predominantly manic) patients with bipolar affective disorder, 20 lithium-treated euthymic patients with bipolar affective disorder, and 11 healthy controls. Results: In both tissues, the immunolabeling of the 45-kd form of **G-alpha** -s was higher in the bipolar affective disorder group considered as a whole (treated or untreated) compared with controls, effects that reached statistical significance in the leukocyte membranes. There were no significant differences in the immunolabeling of **G-alpha** -i1/2, **G-alpha**-q/11, or pertussis toxin-catalyzed (32P)ADP ribosylation in either tissue in the untreated bipolar affective disorder group compared with controls. In both tissues, lithium-treated subjects demonstrated lower levels of **G-alpha**-q/11 and higher levels of pertussis toxin-catalyzed (32P)ADP-ribosylation, which reached significance in the platelet membranes. Conclusions: Our results are complementary to the previously reported findings of elevated **G-alpha**-s levels in postmortem brain tissue from patients with bipolar affective disorder and in mononuclear leukocytes obtained from **depressed** patients with bipolar (but not unipolar) affective disorder. The significantly higher levels of pertussis toxin-catalyzed (32P)ADP ribosylation in the subjects receiving long-term lithium-treatment replicates our findings in rat cortex and in healthy volunteers and adds to the growing body of evidence implicating **G** **-alpha**-i as a target of lithium's actions.
CC Cytology and Cytochemistry - Human *02508
Behavioral Biology - Human Behavior *07004
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066

Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Lipids *13006
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Clinical Pharmacology *22005
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026

BC Hominidae *86215

IT Major Concepts
Behavior; Blood and Lymphatics (Transport and Circulation); Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Nervous System (Neural Coordination); Neurology (Human Medicine, Medical Sciences); Pathology; Pharmacology; Psychiatry (Human Medicine, Medical Sciences)

IT Chemicals & Biochemicals
LITHIUM; **ADENYLATE CYCLASE**

IT Miscellaneous Descriptors
ADENYLATE CYCLASE; ANTIPSYCHOTIC-DRUG; **G PROTEIN ALPHA**-SUBUNIT; LITHIUM; MONONUCLEAR LEUKOCYTE; MOOD-STABILIZING ACTION; PATHOPHYSIOLOGY; PHARMACODYNAMICS; PHOSPHOINOSITIDE TURNOVER

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN 7439-93-2 (LITHIUM)
9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 25 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:131482 BIOSIS
DN PREV199598145782
TI Chronic treatment of C6 glioma cells with **antidepressant** drugs increases functional coupling between a **G protein** (**G**-s) and **adenylyl cyclase**.
AU Chen, Jiang; **Rasenick, Mark M. (1)**
CS (1) Dep. Physiol. Biophysics, Univ. Illinois Coll. Med., 901 S. Wolcott Ave., m/c 901, Chicago, IL 60612-7342 USA
SO Journal of Neurochemistry, (1995) Vol. 64, No. 2, pp. 724-732. ISSN: 0022-3042.
DT Article
LA English
AB It has been reported that **antidepressant** treatment in rats results in a significant increase of **G**-s-mediated **stimulation** of **adenylyl cyclase** and this effect correlates well with the clinical therapeutic response. This increased activity occurs despite a down-regulation of several receptors linked normally to the **stimulation** of that enzyme. To distinguish between these effects and to determine whether presynaptic components of the cell are required, C6 glioma cells were treated with **antidepressants**. Tricyclic (amitriptyline and desipramine) or atypical (iprindole) **antidepressant** exposure to C6 cells for 5 days significantly increased guanylyl-5'-imidodiphosphate (Gpp(NH)p)-**stimulated adenylyl cyclase** activity in membrane preparations in a manner similar to that seen for rat brain membranes after 21-day treatment. This effect was drug dose and exposure time dependent. Nevertheless, **stimulation** of **adenylyl cyclase** by isoproterenol was decreased after

antidepressant treatment. By comparison, the **antidepressant**-induced beta-receptor desensitization occurred earlier than the enhancement of Gpp(NH)p-activated **adenylyl cyclase**, and extensive desensitization of beta receptors by isoproterenol treatment did not enhance the Gpp(NH)p-**stimulated adenylyl cyclase** activity. These results indicated that the **antidepressant** has a direct effect on cell signaling and this enhanced Gpp(NH)p-**stimulated adenylyl cyclase** activity is not correlated with desensitization of beta-adrenergic receptor **stimulated adenylyl cyclase**. These data contribute to the suggestion that **G proteins** (especially **G**-s) are the target of **antidepressant** actions. Immunoblotting showed that neither the number of **G protein** subunits (**alpha**-s, **alpha**-i, **alpha**-o, and beta) nor their association with the plasma membrane was changed after **antidepressant** treatment. Thus, these results are consistent with the hypothesis that chronic **antidepressant** treatment acts directly at the postsynaptic membrane to increase the coupling between **G**-s and **adenylyl cyclase**.

CC Cytology and Cytochemistry - Animal *02506
Behavioral Biology - Animal Behavior *07003
Behavioral Biology - Human Behavior *07004
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Endocrine System - Neuroendocrinology *17020
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Endocrine System *22016
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
Neoplasms and Neoplastic Agents - Biochemistry *24006

BC Hominidae 86215
Muridae *86375

IT Major Concepts
Behavior; Biochemistry and Molecular Biophysics; Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Metabolism; Nervous System (Neural Coordination); Neurology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pathology; Pharmacology; Psychiatry (Human Medicine, Medical Sciences)

IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE; IPRINDOLE

IT Miscellaneous Descriptors
AMITRIPTYLINE; **ANTIDEPRESSANT**-DRUG; BETA-ADRENERGIC RECEPTOR; BRAIN; **DEPRESSION**; DESIPRAMINE; **G**-S **PROTEIN**; GTP BINDING **PROTEIN**; IPRINDOLE; PHARMACODYNAMICS; POSTSYNAPTIC MEMBRANE; RECEPTOR-EFFECTOR COUPLING; TRICYCLIC **ANTIDEPRESSANT** AGENT

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rat (Muridae); Hominidae (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates

RN **9012-42-4 (ADENYLYL CYCLASE)**
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)
5560-72-5 (IPRINDOLE)

L114 ANSWER 26 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:50814 BIOSIS
DN PREV199598065114
TI Augmented **adenylyl cyclase** activation by chronic **antidepressant** treatment of C6 glioma cells is due to facilitated **G protein** coupling.
AU Chen, J.; **Rasenick, M. M.**
CS Dep. Physiol. Biophysics, Univ. Illinois Coll. Med., Chicago, IL 60612-7342 USA
SO Molecular Biology of the Cell, (1994) Vol. 5, No. SUPPL., pp. 21A. Meeting Info.: Thirty-fourth Annual Meeting of the American Society for Cell Biology San Francisco, California, USA December 10-14, 1994 ISSN: 1059-1524.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules 10506
Biophysics - Membrane Phenomena *10508
Enzymes - Chemical and Physical *10806
Nervous System - Physiology and Biochemistry *20504
BC Muridae *86375
IT Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Nervous System (Neural Coordination)
IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE; IPRINDOLE
IT Miscellaneous Descriptors
AMITRIPTYLINE; BETA ADRENERGIC RECEPTOR; DESIPRAMINE; IPRINDOLE; MEETING ABSTRACT; MEETING POSTER
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9012-42-4 (ADENYLYL CYCLASE)**
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)
5560-72-5 (IPRINDOLE)

L114 ANSWER 27 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:472567 BIOSIS
DN PREV199497485567
TI Functional activation of C6 glioma **adenylyl cyclase** by **G-protein** after chronic exposure to **antidepressant** is independent of receptor desensitization.
AU Chen, J.; **Rasenick, M. M.**
CS Dep. Physiol. Biophys., Univ. Illinois Coll. Med., Chicago, IL 60612-7342 USA
SO Society for Neuroscience Abstracts, (1994) Vol. 20, No. 1-2, pp. 436. Meeting Info.: 24th Annual Meeting of the Society for Neuroscience Miami Beach, Florida, USA November 13-18, 1994 ISSN: 0190-5295.
DT **Conference**
LA English

CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals** 00520
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Nervous System - Pathology *20506
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
BC Muridae *86375
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Nervous System (Neural Coordination); Pharmacology
IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE; IPRINDOLE
IT Miscellaneous Descriptors
AMITRIPTYLINE; **ANTIDEPRESSANT**-DRUG; DESIPRAMINE; IPRINDOLE; MEETING ABSTRACT; MEETING SLIDE
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9012-42-4** (**ADENYLYL CYCLASE**)
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)
5560-72-5 (IPRINDOLE)

L114 ANSWER 28 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:117447 BIOSIS
DN PREV199497130447
TI **Adenylyl cyclase** activity and **G-protein** subunit levels in postmortem frontal cortex of suicide victims.
AU Cowburn, Richard F. (1); Marcusson, Jan O.; Eriksson, Anders; Wiehager, Birgitta; O'Neill, Cora
CS (1) Dep. Geriatric Med. B56, Karolinska Inst., Huddinge Univ. Hosp., S-141 86 Huddinge Sweden
SO Brain Research, (1994) Vol. 633, No. 1-2, pp. 297-304.
ISSN: 0006-8993.
DT Article
LA English
AB Basal and **stimulated adenylyl cyclase** activities and **G-s** and **G-i protein** a-subunit levels (**G-salpha** and **G-ialpha**) were compared in postmortem frontal cortex from 18 suicide cases and 22 matched controls. Basal, guanosine 5'-O-(3-thiotriphosphate) (GTP-gamma-S) **stimulated** and forskolin **stimulated** enzyme activities were significantly lower in the suicide cases, compared to controls. These effects were most apparent in those suicides that had died from violent means or that had had a history of **depression** and appeared to reflect the lowered basal activity rather than a reduced ability of either GTP-gamma-S or forskolin to activate the enzyme. No significant correlations were found between **adenylyl cyclase** activity and either subject age or postmortem delay. Western blotting revealed no significant differences in **G-salpha** and **G-ialpha** levels between control and suicide cases. However, levels of the smaller **G-salpha** isoform (**G-salpha**-S) showed a tendency to be increased in the violent death suicide and **depressed** suicide subgroups, compared to controls. Levels of the larger **G-salpha** isoform (**G-salpha**-L) showed a significant positive correlation

with subject age. **G-ialpha**. levels showed a significant negative correlation with subject age and a positive correlation with postmortem delay. These results support the hypothesis that suicidal behaviour and **depressive** illness may be associated with an altered regulation of **adenylyl cyclase**.

CC Behavioral Biology - Human Behavior *07004
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Necrosis *12510
Metabolism - Proteins, Peptides and Amino Acids *13012
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Drug Metabolism; Metabolic Stimulators 22003
Pharmacology - Neuropharmacology *22024

BC Hominidae *86215

IT Major Concepts
Behavior; Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Neurology (Human Medicine, Medical Sciences); Pathology; Psychiatry (Human Medicine, Medical Sciences)

IT Chemicals & Biochemicals
ADENYLYL CYCLASE

IT Miscellaneous Descriptors
DEPRESSION

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN **9012-42-4 (ADENYLYL CYCLASE)**

L114 ANSWER 29 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:50907 BIOSIS
DN PREV199497063907
TI Effect of chronic **antidepressant** treatment on tubulin function in rat brain.
AU Kamada, H. (1); Saito, T. (1); Ozawa, H. (1); Hatta, S.; Hashimoto, E. (1); Ashizawa, T. (1); **Rasenick, M. M.**; Takahata, N. (1)
CS (1) Dep. Neuropsychiatry, Sapporo Med. Univ., Sapporo 060 Japan
SO Society for Neuroscience Abstracts, (1993) Vol. 19, No. 1-3, pp. 939.
Meeting Info.: 23rd Annual Meeting of the Society for Neuroscience Washington, D.C., USA November 7-12, 1993
ISSN: 0190-5295.
DT **Conference**
LA English

CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Nervous System - Pathology *20506
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
Toxicology - Pharmacological Toxicology *22504

BC Muridae *86375

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Nervous System (Neural Coordination); Pharmacology; Toxicology

IT Chemicals & Biochemicals

AMITRIPTYLINE; **ADENYLATE CYCLASE**
IT Miscellaneous Descriptors
ADENYLATE CYCLASE; AMITRIPTYLINE; MEETING ABSTRACT; MEETING POSTER; TOXICITY
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates
RN 50-48-6 (AMITRIPTYLINE)
9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 30 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:4483 BIOSIS
DN PREV199497017483
TI Chronic **antidepressant** treatment changes **G protein** functional interactions without altering **G protein** content.
AU Chen, J.; **Rasenick, M. M.**
CS Dep. Physiol. and Biophys., Univ. Ill. Chicago, Chicago, IL 60612-7384 USA
SO Society for Neuroscience Abstracts, (1993) Vol. 19, No. 1-3, pp. 309.
Meeting Info.: 23rd Annual Meeting of the Society for Neuroscience Washington, D.C., USA November 7-12, 1993
ISSN: 0190-5295.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy *12512
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy 21002
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
BC Muridae *86375
IT Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Nervous System (Neural Coordination); Pathology; Pharmacology
IT Chemicals & Biochemicals
ADENYLYL CYCLASE
IT Miscellaneous Descriptors
ADENYLYL CYCLASE; CEREBRAL CORTEX; MEETING ABSTRACT; MEETING POSTER; PLASMA MEMBRANE
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9012-42-4 (ADENYLYL CYCLASE)**

L114 ANSWER 31 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1992:534656 BIOSIS
DN BR43:120356
TI EFFECTS OF **ANTIDEPRESSANTS** AND ELECTROCONVULSIVE SHOCK ON COUPLING OF **G PROTEIN** TO **ADENYLATE CYCLASE**.

AU OZAWA H; HATTA S; **RASENICK M M**; TAKAHATA N; SAITO T
CS DEP. NEUROPSYCHIATRY, SAPPORO MED. COLL., SAPPORO 060, JAPAN.
SO RACAGNI, G., N. BRUNELLO AND T. FUKUDA (ED.). INTERNATIONAL CONGRESS SERIES, NO. 968. BIOLOGICAL PSYCHIATRY, VOLS. 1 AND 2; PROCEEDINGS OF THE 5TH WORLD CONGRESS OF BIOLOGICAL PSYCHIATRY, FLORENCE, ITALY, JUNE 9-14, 1991. XXVIII+886P.(VOL. 1); XXXI+949P.(VOL. 2) ELSEVIER SCIENCE PUBLISHERS B.V.: AMSTERDAM, NETHERLANDS; (DIST. IN THE USA AND CANADA BY ELSEVIER SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK, USA). ILLUS. (1991) 0 (0), 188-191.
CODEN: EXMDA4. ISSN: 0531-5131. ISBN: 0-444-81410-8 (VOL. 1), 0-444-89295-8 (VOL. 2), 0-444-89296-6 (SET).
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Behavioral Biology - Animal Behavior *07003
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
External Effects - Electric, Magnetic and Gravitational Phenomena *10610
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
Laboratory Animals - General 28002
BC Muridae 86375
IT Miscellaneous Descriptors
RAT MODEL PHARMACOKINETICS PHARMACODYNAMICS GTP ADP
RN 86-01-1 (GTP)
9012-42-4 (ADENYLATE CYCLASE)
58-64-0Q, 7722-76-1Q (ADP)

L114 ANSWER 32 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:460106 BIOSIS
DN BR39:95467
TI ACCELERATED GUANINE NUCLEOTIDE EXCHANGE BETWEEN GI AND **GS** AND ENHANCED COUPLING OF **GS** TO **ADENYLATE CYCLASE** SUBSEQUENT TO CHRONIC **ANTIDEPRESSANT** TREATMENT.
AU OZAWA H; SAITO T; **RASENICK M M**; TAKAHATA N
CS DEP. NEUROPSYCHIATRY, SAPPORO MED. COLL., SAPPORO 060, JPN.
SO NISHIZUKA, Y., M. ENDO AND C. TANAKA (ED.). ADVANCES IN SECOND MESSENGER AND PHOSPHOPROTEIN RESEARCH, VOL. 24. THE BIOLOGY AND MEDICINE OF SIGNAL TRANSDUCTION; 7TH INTERNATIONAL CONFERENCE ON CYCLIC NUCLEOTIDES, CALCIUM AND PROTEIN PHOSPHORYLATION, KOBE, JAPAN, OCTOBER 8-13, 1989. XXXIII+750P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS. (1990) 0 (0), 562.
CODEN: ASMRE5. ISBN: 0-88167-670-5.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
Toxicology - Pharmacological Toxicology *22504

BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT RAT CEREBRAL SYNAPSES DRUG TOXICITY SIGNAL TRANSDUCTION
RN **9012-42-4 (ADENYLATE CYCLASE)**
73-40-5Q, 69257-39-2Q (GUANINE)

L114 ANSWER 33 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:393028 BIOSIS
DN BR39:63989
TI INCREASED COUPLING OF **STIMULATORY G PROTEIN** TO **ADENYLATE CYCLASE** SUBSEQUENT TO CHRONIC ADMINISTRATION OF **ANTIDEPRESSANTS.**
AU OZAWA H; **RASENICK M M**; SAITO T; TAKAHATA N
CS DEP. NEUROPSYCHIATRY, SAPPORO MED. COLL., SAPPORO, JPN.
SO 5TH WORKSHOP FOR THE BIOCHEMICAL AND PHARMACOLOGICAL RESEARCH ON AFFECTIVE DISORDERS, TOKYO, JAPAN, MAY 26-27, 1989. JPN J PSYCHIATRY NEUROL. (1990) 44 (1), 131-132.
CODEN: JJPNEA. ISSN: 0912-2036.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Pharmacology - Clinical Pharmacology 22005
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
BC Muridae 86375
IT Miscellaneous Descriptors
RAT DESIPRAMINE AMITRIPTYLINE IPRINDOLE **ANTIDEPRESSANT** AGENT GTP-BINDING PROTEIN ANIMAL MODEL
RN 50-47-5 (DESIPRAMINE)
50-48-6 (AMITRIPTYLINE)
5560-72-5 (IPRINDOLE)
9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 34 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:120935 BIOSIS
DN BR38:55145
TI CHRONIC **ANTIDEPRESSANT** TREATMENT AUGMENTS COUPLING OF THE GTP BINDING PROTEIN **GS** TO THE CATALYTIC MOIETY OF **ADENYLATE CYCLASE.**
AU OZAWA H; **RASENICK M M**
CS PHYSIOL. AND BIOPHYS., UNIV. ILL. COLL. MED., CHICAGO, ILL. 60680.
SO 19TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, PHOENIX, ARIZONA, USA, OCTOBER 29-NOVEMBER 3, 1989. SOC NEUROSCI ABST. (1989) 15 (1), 853.
CODEN: ASNEE5.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Energy and Respiratory Metabolism *13003
Metabolism - Proteins, Peptides and Amino Acids *13012
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
Laboratory Animals - General 28002
BC Muridae 86375
IT Miscellaneous Descriptors

ABSTRACT RAT
RN **9012-42-4 (ADENYLATE CYCLASE)**

L114 ANSWER 35 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:73865 BIOSIS
DN BA89:41691
TI COUPLING OF THE **STIMULATORY** GTP-BINDING **PROTEIN G**-S TO RAT SYNAPTIC MEMBRANE **ADENYLATE CYCLASE** IS ENHANCED SUBSEQUENT TO CHRONIC **ANTIDEPRESSANT** TREATMENT.
AU OZAWA H; **RASENICK M M**
CS DEP. PHYSIOL. BIOPHYS., UNIV. ILL. CHICAGO COLL. MED., P.O. BOX 6998, CHICAGO, ILL. 60680.
SO MOL PHARMACOL, (1989) 36 (5), 803-808.
CODEN: MOPMA3. ISSN: 0026-895X.
FS BA; OLD
LA English
AB In an attempt to resolve a unified postreceptor mechanism of action for **antidepressant** therapy, rats were treated with amitriptyline, desipramine or iprindole. Chronic treatment with these **antidepressant** drugs increased guanylylimidodiphosphate-[Gpp(NH)p-], NaF-, or forskolin-activated **adenylate cyclase** in synaptic membranes prepared from cerebral cortexes of treated rats. Gpp(NH)p-dependent inhibition of **adenylate cyclase** was unaffected. Maximal binding of the photoaffinity GTP analog azidoanilido-GTP (AAGTP) to the **adenylate cyclase stimulatory** (**Gs.alpha.**) and inhibitory (Gi. **alpha.**) **G proteins** was unaffected by **antidepressant** treatment. The chemical elimination of **Gs** (low pH treatment) eliminated all differences between control and **antidepressant**-treated groups. Further, nonneural tissues from rats receiving chronic **antidepressants** showed no changes in **adenylate cyclase** activity or AAGTP binding. The results of these studies suggest that chronic **antidepressant** administration promoted increased coupling between **Gs** and catalytic unit of **adenylate cyclase**. Thus, the molecular locus of **antidepressant** action may reside at the **stimulatory** GTP-binding **protein, Gs**.
CC Behavioral Biology - Animal Behavior *07003
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Nervous System - Physiology and Biochemistry *20504
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
BC Muridae 86375
IT Miscellaneous Descriptors
AMITRIPTYLINE DESIPRAMINE IPRINDOLE **ANTIDEPRESSANT**-DRUG
GUANYLYLIMIDODIPHOSPHATE **ADENYLATE CYCLASE**
RN 50-47-5 (DESIPRAMINE)
50-48-6 (AMITRIPTYLINE)
5560-72-5 (IPRINDOLE)
9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 36 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1989:22065 BIOSIS
DN BR36:9742
TI ENHANCED COUPLING OF **G PROTEINS** TO **ADENYLATE CYCLASE** SUBSEQUENT TO CHRONIC **ANTIDEPRESSANT** TREATMENT.
AU OZAWA H; **RASENICK M M**
CS DEP. PHYSIOL. BIOPHYSICS, UNIV. ILL. COLL. OF MED., CHICAGO, ILL. 60680.
SO 18TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, TORONTO, ONTARIO,

CANADA, NOVEMBER 13-18, 1988. SOC NEUROSCI ABSTR. (1988) 14 (1), 576.
CODEN: ASNEE5.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids 13012
Nervous System - General; Methods 20501
Nervous System - Pathology *20506
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT RAT AMITRIPTYLINE IMIPRAMINE IPRINDOL
RN 50-48-6 (AMITRIPTYLINE)
50-49-7 (IMIPRAMINE)
9012-42-4 (ADENYLATE CYCLASE)

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FILE 'MEDLINE' ENTERED AT 16:11:13 ON 18 MAR 2002

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=> d all tot l158

L158 ANSWER 1 OF 4 MEDLINE
AN 2000110747 MEDLINE
DN 20110747 PubMed ID: 10646827
TI Platelet alpha2A-adrenoceptor function in major depression: Gi coupling, effects of imipramine and relationship to treatment outcome.
AU Gurguis G N; Vo S P; Griffith J M; Rush A J
CS Mental Health Services, Department of Veterans Affairs Medical Center, Dallas, TX, USA.. gurguis.george@dallas.va.gov
SO PSYCHIATRY RESEARCH, (1999 Dec 20) 89 (2) 73-95.
Journal code: QC4; 7911385. ISSN: 0165-1781.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200002
ED Entered STN: 20000218
Last Updated on STN: 20000218

Entered Medline: 20000208

AB Studies suggest alpha2A-adrenoceptors (alpha(2A)AR) dysregulation in major depressive disorder (MDD). Platelet alpha(2A)ARs exist in high- and low-conformational states that are regulated by Gi protein. Although alpha(2A)AR coupling to Gi protein plays an important role in signal transduction and is modulated by antidepressants, it has not been previously investigated. Alpha2AR density in the high- and low-conformational states, agonist affinity and coupling efficiency were investigated in 27 healthy control subjects, 23 drug-free MDD patients and 16 patients after imipramine treatment using [3H]yohimbine saturation and norepinephrine displacement of [3H]yohimbine binding experiments. Coupling measures were derived from NE-displacement experiments. Patients had significantly higher alpha(2A)AR density, particularly in the high-conformational state, than control subjects. Coupling indices were normal in patients. High pre-treatment agonist affinity to the receptor in the high-conformational state and normal coupling predicted positive treatment outcome. Decreased coupling to Gi predicted a negative treatment outcome. Imipramine induced uncoupling (-11%) and redistribution of receptor density in treatment responders only, but had no effect on alpha(2A)AR coupling or density in treatment non-responders. Increased alpha(2A)AR density may represent a trait marker in MDD. The results provide indirect evidence for abnormal protein kinase A (PKA) and protein kinase C (PKC) in MDD which may be pursued in future investigations.

CT Check Tags: Human; Male; Support, Non-U.S. Gov't
Adrenergic Uptake Inhibitors: PD, pharmacology
*Adrenergic Uptake Inhibitors: TU, therapeutic use
Adult
Antidepressive Agents, Tricyclic: PD, pharmacology
***Antidepressive Agents, Tricyclic: TU, therapeutic use**
Biological Markers: BL, blood
Blood Platelets: DE, drug effects
*Blood Platelets: ME, metabolism
Case-Control Studies
*Depression, Involutional: BL, blood
*Depression, Involutional: DT, drug therapy
Depression, Involutional: PX, psychology
***G-Protein, Inhibitory Gi: BL, blood**
Imipramine: PD, pharmacology
***Imipramine: TU, therapeutic use**
Middle Age
Norepinephrine: ME, metabolism
Protein Binding
Protein Kinases: ME, metabolism
Psychiatric Status Rating Scales
*Receptors, Adrenergic, alpha-2: BL, blood
Receptors, Adrenergic, alpha-2: DE, drug effects
Treatment Outcome
Yohimbine: ME, metabolism

RN 146-48-5 (Yohimbine); 50-49-7 (Imipramine); 51-41-2 (Norepinephrine)

CN 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents, Tricyclic); 0 (Biological Markers); 0 (Receptors, Adrenergic, alpha-2); EC 2.7.1.37 (Protein Kinases); EC 3.6.1.- (**G-Protein**, Inhibitory Gi)

L158 ANSWER 2 OF 4 MEDLINE

AN 2000086845 MEDLINE

DN 20086845 PubMed ID: 10618463

TI Neutrophil beta(2)-adrenoceptor function in major depression: G(s) coupling, effects of imipramine and relationship to treatment outcome.

AU Gurguis G N; Vo S P; Griffith J M; Rush A J

CS The Department of Veterans Affairs Medical Center, Dallas, TX, USA.. gurguis.george@dallas.va.gov

SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1999 Dec 15) 386 (2-3) 135-44. Journal code: EN6; 1254354. ISSN: 0014-2999.

CY Netherlands

DT (CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200002
ED Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000229
AB Abnormal beta(2)-adrenoceptor density and beta(2)-adrenoceptor-mediated cyclic adenosine monophosphate (cAMP) responses were inconsistently reported in major depressive disorder. Tricyclic antidepressants downregulate beta-adrenoceptor density and decrease coupling to **G** (s) **protein**. Abnormal beta-adrenoceptor coupling may exist in major depressive disorder and may relate to treatment response. We investigated beta(2)-adrenoceptor coupling to **G**(s) **protein** in 25 controls, 23 major depressive disorder drug-free patients and 16 major depressive disorder patients after chronic imipramine treatment using agonist displacement experiments. Pretreatment beta(2)-adrenoceptor coupling and density were normal in patients as a whole. Chronic imipramine induced beta(2)-adrenoceptor uncoupling. This effect was observed in treatment responders who had increased beta(2)-adrenoceptor density in the high-conformational state and supercoupling prior to treatment. Beta(2)-adrenoceptor density decreased after imipramine treatment. Treatment non-responders had seemingly normal pretreatment beta(2)-adrenoceptor function, which was not changed by imipramine. Differences in beta(2)-adrenoceptor regulation in major depressive disorder may underlie treatment response. The results indirectly implicate abnormal agonist-mediated beta(2)-adrenoceptor gene expression, **protein** kinase A, and **protein** kinase C in major depressive disorder.
CT Check Tags: Human; Male; Support, Non-U.S. Gov't
Adrenergic Uptake Inhibitors: TU, therapeutic use
Adult
***Antidepressive Agents, Tricyclic: TU, therapeutic use**
***Depression, Involutional: DT, drug therapy**
Depression, Involutional: ME, metabolism
***G-Protein, Stimulatory Gs: ME, metabolism**
***Imipramine: TU, therapeutic use**
Middle Age
Neutrophils: ME, metabolism
*Receptors, Adrenergic, beta-2: ME, metabolism
Regression Analysis
Severity of Illness Index
Treatment Outcome
RN 50-49-7 (Imipramine)
CN 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents, Tricyclic); 0 (Receptors, Adrenergic, beta-2); EC 3.6.1.- (**G-Protein**, Stimulatory **Gs**)

L158 ANSWER 3 OF 4 MEDLINE
AN 1999332548 MEDLINE
DN 99332548 PubMed ID: 10404469
TI Adrenergic receptor function in panic disorder. II. Neutrophil beta 2 receptors: **Gs protein** coupling, effects of imipramine treatment and relationship to treatment outcome.
AU Gurguis G N; Blakeley J E; Antai-Otong D; Vo S P; Orsulak P J; Petty F; Rush A J
CS Department of Veterans Affairs Medical Center, Laboratory of Clinical Neuroscience, Dallas, TX 75216, USA.. gurguis.george@dallas.va.gov
SO JOURNAL OF PSYCHIATRIC RESEARCH, (1999 Jul-Aug) 33 (4) 309-22. Ref: 115
Journal code: JTJ; 0376331. ISSN: 0022-3956.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English

FS Priority Journals
EM 199912
ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991227
AB Panic attacks are associated with increased autonomic symptoms, suggesting increased beta 2-adrenergic receptor (beta 2AR) function in PD. Tricyclic antidepressants downregulate beta AR function. Previous studies on beta AR function in PD, however, are inconsistent. We recently found increased beta AR coupling and density in neutrophils of symptomatic drug-free PD patients. This study evaluated beta AR coupling to **Gs protein** in 28 controls, 25 drug-free PD patients and 8 PD imipramine-treated patients. PD patients had significantly higher coupling and receptor density, particularly in the high-conformational state. Differences were more pronounced in patients with less depressive symptomatology. Treatment with imipramine was associated with decreased beta AR coupling and density in the high-conformational state. Several beta AR binding parameters were related to severity of anxiety symptoms and treatment outcome. Antidepressants downregulate beta AR density and induce uncoupling from **Gs protein** in PD. Future studies may investigate beta AR coupling in relationship to treatment outcome and the role of beta AR kinase in PD.
CT Check Tags: Comparative Study; Human; Male; Support, U.S. Gov't, Non-P.H.S.
*Adrenergic beta-Antagonists: PD, pharmacology
Adult
***Antidepressive Agents, Tricyclic: PD, pharmacology**
***Antidepressive Agents, Tricyclic: TU, therapeutic use**
*Binding, Competitive: DE, drug effects
Cell Count: DE, drug effects
Down-Regulation (Physiology): DE, drug effects
***G-Protein, Stimulatory Gs: DE, drug effects**
***Imipramine: PD, pharmacology**
***Imipramine: TU, therapeutic use**
Middle Age
*Neutrophils: DE, drug effects
Neutrophils: ME, metabolism
Panic Disorder: DI, diagnosis
***Panic Disorder: DT, drug therapy**
Panic Disorder: PX, psychology
Prospective Studies
Psychiatric Status Rating Scales
*Receptors, Adrenergic, beta-2: DE, drug effects
Receptors, Adrenergic, beta-2: ME, metabolism
Severity of Illness Index
Treatment Outcome
RN 50-49-7 (Imipramine)
CN 0 (Adrenergic beta-Antagonists); 0 (Antidepressive Agents, Tricyclic); 0 (Receptors, Adrenergic, beta-2); EC 3.6.1.- (**G-Protein**, Stimulatory **Gs**)

L158 ANSWER 4 OF 4 MEDLINE
AN 1999103182 MEDLINE
DN 99103182 PubMed ID: 9885796
TI Adrenergic receptor function in panic disorder. I. Platelet alpha 2 receptors: Gi protein coupling, effects of imipramine, and relationship to treatment outcome.
AU Gurguis G N; Antai-Otong D; Vo S P; Blakeley J E; Orsulak P J; Petty F; Rush A J
CS Department of Veterans Affairs Medical Center, Dallas, Texas 75216, USA.
SO NEUROPSYCHOPHARMACOLOGY, (1999 Feb) 20 (2) 162-76.
Journal code: ADQ; 8904907. ISSN: 0893-133X.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 199903
ED Entered STN: 19990413
Last Updated on STN: 20000303
Entered Medline: 19990329
AB Various studies suggest alpha 2-adrenergic receptor (alpha 2AR) dysregulation in panic disorder (PD). Platelet alpha 2-AR exist in high- and low-conformational states as a function of their coupling to Gi protein. alpha 2AR coupling is important in signal transduction and is modulated by antidepressants. alpha 2AR density in the high- and low-conformational states, agonist affinity, and coupling efficiency were investigated in 21 healthy controls, 21 drug-free PD patients, and eight imipramine-treated patients using norepinephrine displacement of 3H-yohimbine binding. Percentage of receptors in the high-conformational state (%RH) and the ratio of the agonist dissociation constant to the receptor in the low-/high-conformational state (KL/KH), calculated from displacement experiments, were used as coupling indices. Patients had high alpha 2AR density in both conformational states. %RH and KL/KH ratio were significantly different, particularly in patients with Hamilton scale for depression (HAMD) scores > or = 15. Imipramine treatment (29 weeks) had no effect on alpha 2AR density or coupling, despite improvement in anxiety ratings. High pretreatment alpha 2AR density and coupling predicted low severity of anxiety after treatment. Increased alpha 2AR density and abnormal coupling may represent an adaptive mechanism or trait marker in PD.
CT Check Tags: Human; Male; Support, U.S. Gov't, Non-P.H.S.
Adult
Agoraphobia: BL, blood
Agoraphobia: DT, drug therapy
Agoraphobia: PX, psychology
Antidepressive Agents, Tricyclic: AE, adverse effects
***Antidepressive Agents, Tricyclic: TU, therapeutic use**
Blood Platelets: DE, drug effects
*Blood Platelets: ME, metabolism
Down-Regulation (Physiology): DE, drug effects
***G-Protein, Inhibitory Gi: BL, blood**
Imipramine: AE, adverse effects
***Imipramine: TU, therapeutic use**
*Panic Disorder: BL, blood
*Panic Disorder: DT, drug therapy
Psychiatric Status Rating Scales
Radioligand Assay
*Receptors, Adrenergic, alpha-2: BL, blood
Treatment Outcome
RN 50-49-7 (Imipramine)
CN 0 (Antidepressive Agents, Tricyclic); 0 (Receptors, Adrenergic, alpha-2); EC 3.6.1.- (**G-Protein**, Inhibitory Gi)

=> d his

(FILE 'HOME' ENTERED AT 14:45:38 ON 18 MAR 2002)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 14:45:49 ON 18 MAR 2002
L1 5901 S ADENYLYL(L)CYCLASE
L2 26403 S ADENYLATE(L)CYCLASE

FILE 'REGISTRY' ENTERED AT 14:46:34 ON 18 MAR 2002
L3 1 S 9012-42-4
E ADENYLYL CYCLASE/CN
L4 1 S E10
L5 745 S ADENYLATE (L) CYCLASE
L6 768 S ADENYL (L) CYCLASE
L7 45 S ADENYLYL (L) CYCLASE
L8 766 S L6-L7 NOT L3,L4

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     FILE 'HCAPLUS' ENTERED AT 14:47:51 ON 18 MAR 2002
L9         18651 S L3
L10            3 S L4
L11         1724 S L8
L12         3247 S ADENYL(L)CYCLASE
L13        33314 S L1,L2,L9-L12
L14           99 S L13 (L) TYPE (L) VI
L15            2 S L14 AND ?DEPRESS?
                 E G PROTEIN/CT
                 E E10+ALL
L16         3058 S E3-E5
L17        18566 S E2
L18         3145 S L16,L17 (L) ALPHA
L19         2873 S GS (L) ALPHA
L20         2516 S L18,L19 AND L13
L21            1 S L18,L19 AND L15
L22           59 S L20 AND ?DEPRESS?
L23           93 S GSALPHA
L24           76 S L23 AND L13
L25            2 S L24 AND ?DEPRESS?
L26            2 S L21,L25
L27          356 S L16,L17 AND ?DEPRESS?
L28          147 S L13 AND L27
                 E RASENICK M/AU
L29           75 S E4-E6
                 E DONATI R/AU
L30           15 S E3,E8-E10
                 E TOKI S/AU
L31           23 S E3,E6
L32           42 S L16-L19,L23 AND L29-L31
L33            9 S L32 AND ?DEPRESS?
L34           35 S L32 AND L13,L14
L35            8 S L34 AND ?DEPRESS?
L36           10 S L15,L21,L26,L33,L35
L37         6138 S L13,L14 AND L16-L19
L38           76 S L13,L14 AND L23
L39         3126 S L13,L14 AND GS
L40         6487 S L37-L39
                 E DRUG SCREENING/CT
                 E E3+ALL
L41           26 S L40 AND E2,E1
L42            2 S L40 AND E5+NT
L43           37 S L36,L41-L42
L44           79 S L40 AND CYTOSKEL?
L45          405 S L40 AND PLASMA(L)MEMBRAN?
L46         1682 S L40 AND CELL(L)MEMBRAN?
L47         1805 S L44-L46
                 E DEPRESSION/CT
                 E E4+ALL
L48         4553 S E1,E2
                 E MENTAL DISORDER/CT
                 E E3+ALL
L49        32582 S E4+NT
L50            4 S  L48,L49 AND L47
L51            2 S L50 AND GS?
L52            1 S L51 NOT MICRODIALYSIS
L53           38 S L43,L52
L54           12 S L53 AND ?DEPRESS?
L55           11 S L54 NOT DNA/TI
L56            2 S L55 AND REVIEW
L57            1 S L56 AND HEART
L58           10 S L55 NOT L57
L59           27 S L53 NOT L55
L60           10 S L58 AND (G OR GS)(L)PROTEIN
L61            8 S L58 AND STIMUL?
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L62           6 S L58 AND ALPHA
L63          10 S L60-L62 AND L1,L2,L9-L62
                E BIPOLAR DISORDER/
                E BIPOLAR DISORDER/CT
                E E3+ALL
L64         784 S E1,E2
                E MANIA/CT
                E E3+ALL
L65         386 S E1,E2
                E PSYCHOSIS/CT
                E E3+ALL
L66        1299 S E1,E2
                E DEMENTIA/CT
                E E3+ALL
L67        2729 S E1,E2
L68          34 S L64-L67 AND L13,L14
L69          31 S L68 AND L1,L2,L16-L19,L23
L70          15 S L68 AND (G OR  GS)(L)PROTEIN
L71           8 S L68 AND GS?
L72          32 S L70,L71,L69
L73          28 S L72 NOT 3/SC
                SEL DN 10 11
L74           2 S L73 AND E1-E2
L75          12 S L63,L74 AND L1,L2,L9-L74
L76          12 S L75 AND (?DEPRESS? OR BIOPOLAR(L)DISORDER OR MENTAL OR GS? OR
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 15:26:06 ON 18 MAR 2002
L77           5 S E3-E7

     FILE 'REGISTRY' ENTERED AT 15:26:42 ON 18 MAR 2002

     FILE 'HCAPLUS' ENTERED AT 15:26:54 ON 18 MAR 2002

     FILE 'BIOSIS' ENTERED AT 15:28:07 ON 18 MAR 2002
                E RASENICK M/AU
L78         164 S E3-E5
                E DONATI R/AU
L79          42 S E3,E5,E7
                E TOKI S/AU
L80          80 S E3,E6
L81       37345 S L13,L14
L82         403 S GSALPHA?
L83        1345 S GS(L)ALPHA
L84       19075 S G(L)PROTEIN(L)?ALPHA?
L85        2014 S L81 AND L82-L84
L86          92 S L78-L80 AND L81
L87          60 S L78-L80 AND L82-L84
L88          30 S L86 AND L87
L89          71 S L86,L87 AND 00520/CC
L90          70 S L86,L87 AND CONFERENCE/DT
L91          50 S L86,L87 NOT L89,L90
L92          25 S L91 NOT ARTICLE/DT
L93          72 S L89,L90
L94           7 S L93 AND L88
L95           4 S L94 AND ?DEPRESS?
L96          21 S L93 AND ?DEPRESS?
L97          21 S L95,L96
L98          13 S 22026/CC AND L97
L99      761781 S 21?/CC
L100     150775 S 22026/CC
L101        335 S L99,L100 AND L82-L84
L102         57 S L101 AND L81
L103         18 S L102 AND ?DEPRESS?
L104          4 S L103 AND 00520/CC
L105          4 S L103 AND CONFERENCE/DT
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L106          15 S L98,L104,L105
L107           7 S L97 NOT L106
L108          22 S L106,L107
L109          53 S L102 NOT L108
L110          14 S L109 AND ?DEPRESS?
L111          36 S L108,L110
L112          34 S L111 AND (G(L)PROTEIN OR GS? OR ALPHA OR STIMUL?)
L113           2 S L111 NOT L112
L114          36 S L111-L113 AND L78-L113

     FILE 'BIOSIS' ENTERED AT 15:41:11 ON 18 MAR 2002

     FILE 'WPIX' ENTERED AT 15:45:03 ON 18 MAR 2002
L115         314 S L1,L2,L12
L116           4 S L115 (L) TYPE (L) VI
L117           6 S ADENYLCYCLASE OR ADENYLYLCYCLASE OR ADENYLATECYCLASE
L118         318 S L115,L116,L117
L119       36926 S GSALPHA? OR GS(L)ALPHA OR (GS OR G)(L)PROTEIN
L120          90 S L118 AND L119
L121           8 S L120 AND ?DEPRESS?
                 E RASENICK M/AU
                 E DONATI R/AU
L122           4 S E3,E4
                 E TOKI S/AU
L123          29 S E3
L124           1 S L122,L123 AND L118,L119
L125        2184 S G PROTEIN
L126           9 S GS PROTEIN
L127          42 S  GSALPHA? OR GS(L)ALPHA
L128         139 S L125 (L)ALPHA
L129          40 S L125-L128 AND L118
L130      111169 S (N102 OR P831)/M0,M1,M2,M3,M4,M5,M6
L131          31 S L130 AND L129
L132           2 S L131 AND ?DEPRESS?

     FILE 'CONFSCI' ENTERED AT 15:55:03 ON 18 MAR 2002
L133        1252 S L118
L134          22 S L133 AND L125-L128

     FILE 'MEDLINE' ENTERED AT 15:56:19 ON 18 MAR 2002
L135       29378 S L118
L136           0 S L3 OR L4
L137        4742 S L135 AND L119
                 E G PROTEIN/CT
                 E E4+ALL
                 E E2+ALL
L138        1872 S E19+NT AND L119
L139        6203 S L137,L138
L140         136 S F3./CT AND L139
                 E GTP-BINDING PROTEINS/CT
                 E E3+ALL
L141          61 S E14 AND L140
L142         494 S E41
L143          22 S L142 AND L140
L144          10 S L143 AND ?DEPRESS?
                 E DEPRESSIVE DISORDER/CT
                 E E3+ALL
L145       53454 S E3+NT
L146          40 S L145 AND L139
L147           1 S L146 AND SCREEN?
L148          93 S L141,L143,L144,L146
L149          53 S L148 AND ?ALPHA?
                 E RASENICK M/AU
L150          60 S E4,E5
                 E DONATI R/AU
L151          29 S E3,E5
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                E TOKI S/AU
L152          93 S E3
L153          44 S L150-L152 AND L135-L149
                E ANTIDEPRESSIVE AGENTS/CT
L154       71720 S E3+NT
L155          59 S L154 AND L137,L139,L143
L156           4 S TREATMENT OUTCOME/CT AND L155
L157           4 S TREATMENT OUTCOME+NT/CT AND L155
L158           4 S L156,L157
L159           8 S L155 AND L153
L160          47 S L155 NOT L156-L159

     FILE 'MEDLINE' ENTERED AT 16:11:13 ON 18 MAR 2002
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